

Use of Buprenorphine in the Pharmacologic Management of Opioid Dependence

A Curriculum for Physicians

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Overview

Overview

Use of Buprenorphine in the Pharmacologic Management of Opioid Dependence: A Curriculum for Physicians

This document is a teaching companion to the CSAT publication, “Buprenorphine Clinical Practice Guidelines.” Its purpose is to assist in preparing lectures and other medical education activities related to office-based prescribing of the medication buprenorphine for the treatment of opioid dependence.

This curriculum includes the core information unique to buprenorphine and its use in the pharmacological management of opioid dependence, as well as a comprehensive overview of treatment for opioid dependence. It does not describe a standard of care. Treatment decisions should be made based upon the individual patient and the level of available resources. This guide provides slides annotated with notes, references and case illustrations.

This curriculum is intended to support the expansion of treatment for opioid dependence into additional settings and to involve new providers. Increasing access to treatment beyond the existing system of licensed methadone programs will increase the number of patients treated.

Office-based treatment for opioid dependence is being developed to address several needs in accordance with public health objectives:

- to increase access to treatment;
- to offer treatment to patients outside the traditional methadone clinic system;
- to mainstream the treatment of opioid dependence by coordinating it with treatment of other medical conditions.

Integrating treatment for opioid dependence into the mainstream of the health care delivery system will increase the likelihood that a patient’s other medical conditions will be addressed. Several such conditions have important public health ramifications, such as tuberculosis, hepatitis C, HIV, and sexually transmitted diseases.

While the material provided in the slides is detailed, this is not a substitute for the clinical experience of a qualified lecturer. Such experience by a clinician provides an important perspective in the delivery of lecture material and in the answers to questions, and can only be partially captured in these slides and notes.

The need for opioid dependence treatment far exceeds what is currently available; office-based buprenorphine is intended to address unmet treatment need, and to place it in the mainstream of medical care. This curriculum provides content to aid the clinician preparing to treat opioid dependent patients in the office; it is best when used with the companion Guidelines and when delivered by clinicians experienced in the treatment of opioid dependence.

Educational Objectives

After participating in a course based on this curriculum, the Addiction Medicine/Psychiatry specialist should be able to:

Overall

1. Identify the clinically relevant pharmacological characteristics of buprenorphine.
2. Describe the resources needed to set up office-based treatment with buprenorphine for patients with opioid dependence.

Basic and Applied Pharmacology

3. Distinguish between spontaneous withdrawal and precipitated withdrawal.
4. Describe and contrast the functions of full agonists, partial agonists, and antagonists.

Non-Pharmacological Treatments

5. Describe the basic approach used in at least four different types of non-pharmacological treatment.

Psychiatric and Medical Co-Morbidities

6. Describe three symptoms of opioid withdrawal or intoxication that mimic symptoms of a psychiatric disorder.

Special Treatment Populations

7. List three special treatment considerations associated with adolescent, opioid dependent patients.
8. List four factors to consider in evaluating a pregnant, opioid dependent woman.

Patient Assessment and Selection

9. List the criteria for establishing the diagnosis of opioid dependence.
10. Describe at least five factors to consider in determining if the patient is an appropriate candidate for office-based treatment with buprenorphine.

Clinical Management

11. Describe at least five areas, which should be covered in the rules and expectations, which are communicated to patients during the patient assessment process.

Patient Confidentiality

12. List at least three situations in which patient information, with patient identity, can be shared under current laws protecting the patient's confidentiality.

Office Management

13. Describe at least three elements, which must be part of the system for urine testing in order for the procedures to be clinically valid.

Medical Record Keeping

14. Describe five key elements of the medical record.
15. List three groups that may scrutinize the medical record.

Introduction

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- I. Overview of opioid abuse and its treatment
- II. Purpose of this curriculum
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Overview of Opioid Abuse and Its Treatment

Epidemiology of opioid abuse

Gaps in current treatment of opioid dependence

Rationale for opioid agonist medications

Epidemiology of Opioid Abuse

Prevalence

2.4 million Americans reported using heroin at least once (1998)

149,000 new users (1999)

980,000 persons using heroin at least weekly (1998)

810,000 chronic users of heroin

1. According to the National Household Survey on Drug Abuse, in 1998, 2,371,000 persons reported ever using heroin, and in 1999, 149,000 reported initiating use. Among the latter, 42,000 were between the ages of 12-17 years, and 73,000 between the ages of 18-25 years.
2. It is also estimated, based on the National Household Survey on Drug Abuse and the Drug Use Forecasting program, that there were 980,000 people who use heroin at least once per week, and 253,000 people who use heroin less than once per week in the United States in 1998.
3. The Office of National Drug Control Policy reports that there are 810,000 chronic opioid users in the United States, and that this is the highest number since the late 1970s.

[References:

National Drug Control Strategy: 2000 Annual Report. Office of National Drug Control Policy, page 116.

National Household Survey on Drug Abuse, Population Estimates 1998. Substance Abuse and Mental Health Services Administration, Office of Applied Studies, Rockville, Maryland, 1999.

Office of National Drug Control Policy. What America's Users Spend on Illegal Drugs: 1988-1995. Washington, DC: Office of National Drug Control Policy 1997.

Summary of Findings from the 1999 National Household Survey on Drug Abuse. Substance Abuse and Mental Health Services Administration, Office of Applied Studies, Rockville, Maryland, 2000.

Web sites: Substance Abuse and Mental Health Services Administration (www.samhsa.gov); National Institute on Drug Abuse (www.nida.nih.gov)]

Epidemiology of Opioid Abuse

Impact of opioid dependence

1991-1995:

Emergency room visits related to heroin increased
from 36,000 to 72,000

Opioid-related deaths increased from 2300 to 4000

[Reference:

Substance Abuse and Mental Health Services Administration (SAMHSA). Drug Abuse Warning Network Series: Year-End Preliminary Estimates From the 1996 Drug Abuse Warning Network Rockville, Maryland: Department of Health and Human Services, Substance Abuse and Mental Health Services Administration; 1997.]

Overview of Opioid Abuse and Its Treatment

Epidemiology of opioid abuse

Gaps in current treatment of opioid dependence

Rationale for opioid agonist medications

Gaps in current treatment of opioid dependence

810,000 chronic opioid users

180,000± patients receiving methadone or LAAM

Detoxification of limited long-term effectiveness

Access to treatment restricted

1. A survey conducted by the American Methadone Treatment Association (AMTA) at the end of 1998 found there were 179,329 patients in methadone treatment.
2. Treatment with methadone is restricted to licensed treatment programs. There are 947 methadone maintenance programs registered with the DEA, and in many locations it has been difficult for new programs to start or existing programs to expand.
3. This difference between the number of patients in treatment and the number of persons who chronically use opioids highlights the need to expand treatment capacity.

[Reference: American Methadone Treatment Association: News Report (sixth edition). American Methadone Treatment Association, New York, December, 1999.]

Overview of Opioid Abuse and Its Treatment

Epidemiology of opioid abuse

Gaps in current treatment of opioid dependence

Rationale for opioid agonist medications

Rationale for opioid agonist medications

Biologic changes in the brain with opioid dependence

Provide insight into the chronic and relapsing nature of opioid dependence

Result from repeated exposure to opioids

Lead to neuronal adaptations in brain resulting in tolerance, physical dependence, craving

Form the basis for pharmacotherapies

Rationale for opioid agonist medications

Opioid agonist maintenance treatment

Targets biological factors perpetuating heroin administration

Prevents withdrawal

Reduces craving

Blocks or attenuates euphoric effects of exogenous opioids

1. When properly dosed and managed, methadone (and LAAM and buprenorphine) prevents opioid withdrawal, reduces craving, and blocks or attenuates the euphoric effects of other opioids such as heroin.

Rationale for opioid agonist medications

Advantages of opioid agonist medication over heroin

Non-parenteral administration

Known composition

Gradual onset and offset

Long-acting

Mildly reinforcing

Medically supervised

1. Medications such as methadone, LAAM and buprenorphine have several advantages over heroin. They can be administered by safer routes (oral or sublingual, rather than by injection); they are long-acting (so that dosing is daily or several times per week, rather than several times per day); they have known composition (so that dosing can be quantified and constant, and so that contaminants are eliminated and there is a known level of purity); their onset of action is gradual and their effects are mildly reinforcing (ensuring compliance in taking the medication while decreasing abuse potential); and they are managed under medical supervision.

Rationale for opioid agonist medications

Opioid agonist treatment

Most effective treatment for opioid dependence

Controlled studies have shown significant:

Decreases in illicit opioid use

Decreases in other drug use

Decreases in criminal activity

Decreases in needle sharing

Improvements in prosocial activities

Improvements in mental health

1. The prototypic opioid agonist maintenance medication is methadone, which will be reviewed later in this section. Controlled studies have shown that methadone, when delivered properly, can be a highly effective medication. Improvements among opioid dependent patients treated with methadone are not limited to decreases in illicit opioid use. Methadone treatment can result in significant decreases in other drug use, and improvements in other areas (such as employment). Further information about methadone (and LAAM) will be provided in a later section.

[References:

Ball J.C., Ross A. The Effectiveness of Methadone Maintenance Treatment. Springer-Verlag, New York, 1991; pages 166-168; 181-182.

Caplehorn J.R.M., Bell J., Kleinbaum D.G., Gebiski V.J. Methadone dose and heroin use during maintenance treatment. *Addiction* 88:119-124, 1993.

Ling W., Charuvastra C., Kaim S.C., Klett J. Methadyl acetate and methadone as maintenance treatments for heroin addicts. *Arch Gen Psychiatry* 33:709-720, 1976.

Simpson D.D., Sells S.B. Opioid Addiction and Treatment: A 12-Year Follow-up. Robert E. Krieger Publishing Company, Malabar, Florida, 1990.

Strain E.C., Stitzer M.L. Methadone Treatment for Opioid Dependence. Johns Hopkins University Press, Baltimore, Maryland, 1999.

Strain E.C., Stitzer M.L., Liebson I.A., Bigelow G.E. Randomized controlled trial of moderate versus high dose methadone in treatment of opioid dependence. *JAMA* 281:1000-1005, 1999.]

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Purpose of this curriculum

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Purpose of this curriculum

This curriculum includes the core information unique to buprenorphine and its use in the pharmacological management of opioid dependence, as well as a comprehensive overview of treatment for opioid dependence. It does not describe a standard of care. Treatment decisions should be made based upon the individual patient and the level of available resources.

1. This guide provides:
 - Slides annotated with notes
 - References
 - Case illustrations

Purpose of this curriculum

This curriculum is intended to support the expansion of treatment for opioid dependence into additional settings and to involve new providers.

1. Increasing access to treatment beyond the existing system of licensed methadone programs will increase the number of patients treated.

Purpose of this curriculum

Office-based treatment for opioid dependence is being developed to address several needs in accordance with public health objectives:

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Summary

The need for opioid dependence treatment far exceeds what is currently available; office-based buprenorphine is intended to address unmet treatment need, and to place it in the mainstream of medical care

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Legislation

Overview to the
Drug Addiction Treatment Act of 2000 –
An Amendment
to the Controlled Substances Act
(October, 2000)

This section provides an overview to the legislative changes that allow for office-based treatment of opioid dependence with controlled substances (i.e., buprenorphine).

It is important for the practitioner to understand these changes, since the clinician will be required to comply with them and to notify the Secretary of Health and Human Services (HHS) before beginning to use buprenorphine in the office setting for the treatment of opioid dependence.

1. HHS and DEA can cancel the authorization for this treatment modality. Legislative action is not needed to repeal the law.

Amended Controlled Substances Act

Revision in legislation allows practitioner to prescribe narcotic drugs in schedule III, IV, V, or combinations of such drugs, for the treatment of opioid dependence

Drugs and practitioner must meet certain requirements

1. Note that the legislation does not specify buprenorphine, but it has been designed with buprenorphine in mind.
2. Also note that the legislation applies only to schedule III, IV and V medications. Methadone and LAAM are schedule II, so this amendment does not apply to them.
3. The requirements of the drug and the practitioner are described on the following slides.

Amended Controlled Substances Act

Practitioner requirements:

“Qualifying physician”

Has capacity to refer patients for appropriate counseling
and ancillary services

No more than 30 patients (individual or group practice)

1. The practitioner must be a “qualifying physician” (as defined in a moment), AND must have the capacity to refer patients for appropriate counseling and ancillary services, AND cannot treat more than 30 patients.
2. The limit on the number of patients that can be treated applies to both an individual physician (solo practice) and to group practices. For example, a group of six physicians can treat only 30 patients. It is possible for this restriction to change – the Secretary can create by regulation different limits for a group practice. However, this has not been done (as of January, 2001).

Amended Controlled Substances Act

“Qualifying physician”:

A licensed physician who meets one or more of the following:

1. Board certified in Addiction Psychiatry
2. Certified in Addiction Medicine by ASAM
3. Certified in Addiction Medicine by AOA
4. Investigator in buprenorphine clinical trials

1. A person can be a “qualifying physician” if he/she fulfills any one of seven criteria (which are continued on the next slide).

Amended Controlled Substances Act

“Qualifying physician” (continued):

Meets one or more of the following:

5. Has completed 8 hours training provided by ASAM, AAAP, AMA, AOA, APA (or other organizations which may be designated by HHS)
6. Training/experience as determined by state medical licensing board
7. Other criteria established through regulation by the Secretary of Health and Human Services

1. This curriculum has been designed to address the 8 hours of training designated as one of the criteria for becoming a “qualifying physician.”

Amended Controlled Substances Act

Practitioner:

Must notify the Secretary of HHS in writing:

His/her name

DEA registration

If in a group practice, names of others in the practice
and DEA registrations

1. The practitioner must then submit, in writing, his/her name, DEA registration, and the names and DEA registrations of other members of the group practice (if applicable). Note the practitioner does not need to provide anything else in writing (e.g., evidence of availability of ancillary services).

Amended Controlled Substances Act

Practitioner:

HHS has 45 days to determine if the physician meets all the requirements

The Attorney General will assign an identification (DEA) number to the practitioner; this number is assigned after 45 days if HHS does not act

1. As stated in the legislation:

“Upon receiving a notification under subparagraph (B), the Attorney General shall assign the practitioner involved an identification number under this paragraph for inclusion with the registration issued for the practitioner pursuant to subsection (f). The identification number so assigned shall be appropriate to preserve the confidentiality of patients for whom the practitioner has dispensed narcotic drugs under the waiver under subparagraph (A).”

2. At this time (January, 2001), it is not clear if the practitioner will receive a new DEA number, or an additional DEA number specific for buprenorphine prescribing.

3. For a practitioner who submits a notification and reasonably believes that the conditions specified in the Act have been met, after 45 days have elapsed from the date the Secretary receives the notification the practitioner can be considered to have a waiver (unless otherwise notified by the Secretary).

Amended Controlled Substances Act

Practitioner:

Violations will put the physician's DEA registration at risk

1. If the practitioner is not registered and dispenses schedule III, IV, or V medications (or combinations of these medications) for maintenance or detoxification purposes, then:

“...the Attorney General may, for purposes of section 304(a)(4), consider the practitioner to have committed an act that renders the registration of the practitioner... to be inconsistent with the public interest.”

Amended Controlled Substances Act

Narcotic drug:

Approved by the FDA for use in maintenance or
detoxification treatment of opioid dependence

Schedule III, IV, or V

Drugs or combinations of drugs

1. Note that no medication is approved as of January, 2001.

Amended Controlled Substances Act

Treatment Improvement Protocol:

Legislation requires the Secretary of HHS (i.e., CSAT) to issue a Treatment Improvement Protocol within 120 days (i.e., mid-February, 2001)

To contain guidelines for treatment and maintenance of opioid dependent patients

That document is the “Buprenorphine Clinical Practice Guidelines”

1. A draft form of the Guidelines is available as of January, 2001.

Amended Controlled Substances Act

Methadone treatment programs:

Practitioner can also prescribe these drugs (i.e., schedule III, IV, or V; approved for maintenance or detoxification treatment) under a methadone program registration

No limit on number of patients when used in the methadone treatment program setting

1. Finally, it is worth noting that the Amendment also allows the practitioner to use buprenorphine in licensed methadone (or LAAM) treatment programs. Furthermore, there is no limit on the number of patients treated when these drugs are used under a methadone (or LAAM) treatment program registration.

Amended Controlled Substances Act

State legislation:

A state may not preclude a practitioner from dispensing or prescribing buprenorphine for opioid dependence treatment unless the state enacts a law prohibiting the practitioner from doing so

1.

Amended Controlled Substances Act

Evaluation period:

During the first three years, HHS and DEA will evaluate safety and efficacy

Safety includes protection of the public health against diversion of the drug

1.

Amended Controlled Substances Act

HHS will evaluate:

Whether the treatment is effective in the office setting

Whether access to treatment has been increased

Whether there has been adverse consequences for the public health

1.

Amended Controlled Substances Act

DEA will evaluate:

The extent of violations of the 30 patient limit

The extent of diversion of the medication

1.

Amended Controlled Substances Act

Evaluation period:

On the basis of these evaluations, HHS and DEA can decide the law should not remain in effect

The law will cease to be in effect in 60 days if such a decision is published

1. HHS and DEA can cancel the authorization for this treatment modality. Legislative action is not needed to repeal the law.

Summary

Legislation sets up relatively minor requirements for a physician to provide office-based buprenorphine treatment of opioid dependence

However, if difficulties arise with buprenorphine (e.g., diversion, misuse), it will be relatively easy for government agencies to end office-based treatment of opioid dependence with buprenorphine

Important for physicians to know and abide by the rules – not risk losing this valuable treatment option

1. HHS and DEA can cancel the authorization for this treatment modality. Legislative action is not needed to repeal the law.

Basic Pharmacology

Basic Pharmacology

1. Buprenorphine has an unusual pharmacological profile. In order to understand buprenorphine's clinical features, it is helpful to understand buprenorphine's pharmacological profile.
2. There are two goals to this section. First, this section reviews general aspects of opioid pharmacology, and second, it applies these general aspects of opioid pharmacology to characterize buprenorphine's pharmacological profile. By understanding buprenorphine's pharmacological effects, it is then easier to understand its clinical use in the treatment of opioid dependence.

Outline for This Talk

- I. General opioid pharmacology
- II. Pharmacology of buprenorphine
- III. Pharmacology of buprenorphine/naloxone
- IV. Summary

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- I. General opioid pharmacology
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1. We'll begin with a brief review of general opioid pharmacology.

Opioids

Opioids constitute a class of drugs found within opium as well as semisynthetic and synthetic compounds that resemble the structure and/or function of these naturally occurring forms.

They are medically used for relief of pain and cough suppression, and many have an abuse potential.

1. The class of opioid drugs includes those that occur naturally (as alkaloids found in opium – for example, morphine), semisynthetic opioids (i.e., derived from naturally occurring opioids – for example, heroin), and synthetic opioids (for example, methadone).
2. While primarily used as analgesics, opioids can also have other indications (e.g., cough suppression, treatment of diarrhea).
3. Opioids are highly reinforcing and have an abuse potential. When an acute dose is administered intravenously for the first time (i.e., in a person with no history of opioid abuse), the person can initially have a feeling of nausea and sickness followed by vomiting. People who subsequently abuse and become dependent upon opioids report retrospectively that, after vomiting, they then felt a high effect (and report that the experience is paradoxically a “pleasant sick”). People who abuse opioids have reported an initial rush in the lower abdomen within the first 1-2 minutes (resembling an orgasm), accompanied by flushing of the skin. They then feel as though they are floating with a feeling of intoxication and euphoria. Drowsiness (or “nodding”) then occurs.

General Opioid Pharmacology

Opioid receptors

The functions of drugs at receptors

Repeated administration and withdrawal of opioid drugs

Affinity and dissociation

Characteristics of drugs with abuse potential

1. Let's begin by reviewing the different types of opioid receptors.

Opioid Receptors

Types of opioid receptors:

Mu

Kappa

Delta

1. There are multiple types of opioid receptors: mu, kappa, and delta receptors plus subtypes for these main classes of opioid receptors. We will not discuss subtypes in this section, as they are not relevant.
2. The prototypic mu agonist opioid is morphine. Activation of the mu receptor can produce a variety of effects, including analgesia, respiratory depression, pupillary constriction, and euphoria.
3. The prototypic kappa agonist opioid is ketocyclazocine (which is no longer available). Kappa activation produces analgesia – as does mu activation – and there was hope that pure kappa agonists might be effective analgesics with lower abuse potential than mu agonist opioids. Unfortunately, kappa activation also appears to produce psychotomimesis in humans.
4. Delta receptors were first isolated from the mouse deferens. There are no prototypic delta agonists studied in humans, and isolated delta activation in humans has not been well characterized.
5. The addictive effects of opioids occur through activation of mu receptors.
6. The role of kappa and delta receptors in the addictive process is not well defined.

Opioid Receptors

Drugs and medications that activate mu receptors:

- morphine
- heroin
- methadone
- LAAM
- hydromorphone
- buprenorphine
- codeine
- fentanyl

1. These are not all the medications that can activate the mu receptor.

General Opioid Pharmacology

Opioid receptors

The functions of drugs at receptors

Repeated administration and withdrawal of opioid drugs

Affinity and dissociation

Characteristics of drugs with abuse potential

1. Next, let's review the different functions that drugs can exert at these receptors.

Functions of Drugs at Receptors

Full agonists:

Occupy the receptor and activate that receptor
Increasing doses of the drug produce increasing receptor-specific effects until a maximum effect achieved
Most abused opioids are full agonists
Examples of full agonist opioids: heroin, LAAM, methadone, morphine

1. A full agonist opioid occupies the receptor and activates that receptor.
2. As the dose of the full agonist is increased, the effect also increases. The effects could include analgesia, respiratory depression, constipation, etc.
3. Eventually a maximum effect is reached – no further effects are produced, even with administration of higher doses.
4. Examples of full mu agonist opioids are methadone, morphine, heroin, and LAAM.

Functions of Drugs at Receptors

Partial agonists:

Bind to and activate receptor

Increasing dose does not produce as great an effect as does increasing the dose of a full agonist (less of a maximal effect is possible)

1. A partial agonist binds to the receptor and activates the receptor (like a full agonist).
2. At lower doses, a partial agonist and a full agonist produce similar effects.
3. However, as the dose of a partial agonist is increased, the effect produced does not increase. There is less of a maximal effect – no matter how much the dose is increased.
4. Buprenorphine is a partial mu agonist opioid, as will be discussed in more detail later.

Functions of Drugs at Receptors

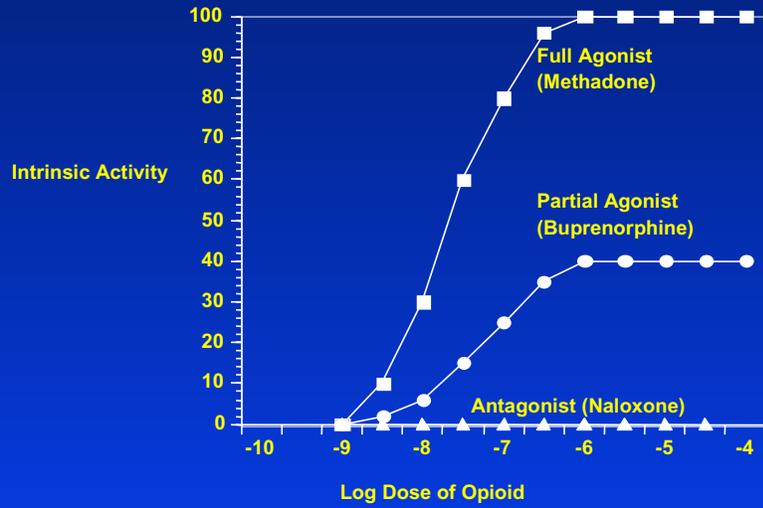
Antagonists:

Bind to receptors but don't activate the receptor

Block the receptor from activation by full and partial agonists

1. An antagonist binds to a receptor but does not activate the receptor. By occupying a receptor, it prevents other drugs such as agonists from occupying and activating that receptor.
2. Examples of opioid antagonists are naloxone (Narcan), naltrexone (ReVia), and nalmeffene.
3. In a person who is not physically dependent upon opioids, an antagonist produces no effects.
4. In a person who is dependent upon opioids, an antagonist can precipitate withdrawal (as reviewed later in this talk).
5. In a person maintained on an antagonist, administration of a full or partial agonist does not result in an effect from the agonist. This is because the antagonist blocks the receptor.
6. Opioid antagonists also appear to be effective in the treatment of some patients with alcohol dependence. This topic will not be reviewed here.

Intrinsic Activity: Full Agonist (Methadone), Partial Agonist (Buprenorphine), Antagonist (Naloxone)



General Opioid Pharmacology

Opioid receptors

The functions of drugs at receptors

Repeated administration and withdrawal of opioid drugs

Affinity and dissociation

Characteristics of drugs with abuse potential

1. Next let's discuss the effects produced by repeated administration of opioids (that is, the production of physical dependence and tolerance), and then the effects when opioids are withdrawn.

Repeated Administration and Withdrawal

Repeated administration of opioids that activate the mu receptor results in dose-dependent physical dependence and tolerance

Physical dependence and tolerance manifest as characteristic withdrawal signs and symptoms upon reduction or cessation of opioid use/administration (the opioid withdrawal syndrome)

1. Repeated administration of an agonist opioid can result in physical dependence. Physical dependence needs to be distinguished from a syndrome of dependence (as is described in DSM-IV). While the term “dependence” is used in both cases, they are different. Physical dependence indicates there has been some physiological change or adaptation in an organism, in response to repeated administration of a drug. A “syndrome of dependence” is a group of signs and symptoms indicating a pattern of pathologic use or “addiction.” The latter can include symptoms such as loss of control over use of the drug, use despite adverse consequences, and a compulsive pattern to use. People can have physical dependence – for example, resulting from chronic use of opioids in a person who has cancer – but not have a syndrome of dependence.

While physical dependence is one possible feature of the syndrome of dependence, it is not the only feature (and is not a required feature). Thus, a person can have a syndrome of dependence (problematic use), without being physically dependent on the substance.

2. Tolerance is another feature of repeated administration of some drugs (such as a mu agonist opioid). Tolerance is the phenomenon of diminishing effect from the same dose of a drug that has been given repeatedly. Alternately, tolerance can be understood as the need for greater doses of the drug to produce the same effect.

3. Physical dependence and tolerance are dose related.

Repeated Administration and Withdrawal

Signs and symptoms of opioid withdrawal:

Dysphoric mood
Nausea or vomiting
Muscle aches/cramps
Lacrimation
Rhinorrhea
Pupillary dilation

1. Physical dependence is typically shown through the demonstration of the opioid withdrawal syndrome when opioid use stops or decreases significantly.
2. The signs and symptoms of the opioid withdrawal syndrome have been well characterized. They are listed on this and the next slide.
3. Withdrawal off short-acting opioids (such as heroin) has been characterized as occurring over a series of stages:

Anticipatory (3-4 hours after last use)

Signs and symptoms: fear of withdrawal, anxiety, drug-seeking behavior

Early (8-10 hours after last use)

Signs and symptoms: anxiety, restlessness, yawning, nausea, sweating, nasal stuffiness, rhinorrhea, lacrimation, dilated pupils, stomach cramps, drug-seeking behavior

Fully-developed (1-3 days after last use)

Signs and symptoms: severe anxiety, tremor, restlessness, piloerection, vomiting, diarrhea, muscle spasm, muscle pain, increased blood pressure, tachycardia, fever, chills, impulse-driven drug-seeking behavior

Repeated Administration and Withdrawal

Signs and symptoms of opioid withdrawal (continued):

Sweating, piloerection

Diarrhea

Yawning

Mild fever

Insomnia

Craving

Distress/irritability

1. Not all of these signs and symptoms need to be present in order to establish the diagnosis of withdrawal. However, it is worth watching the person who has complaints of opioid withdrawal but no physical evidence of withdrawal (especially if they are seeking opioids). Some will complain that they are in opioid withdrawal in an effort to get a prescription for opioids. Watching for objective signs of withdrawal can help determine if they truly are physically dependent on opioids.

2. Opioid withdrawal is not life threatening for healthy adults (for example, compared to the withdrawal syndrome from alcohol, which can be life threatening if untreated). Of course, in the patient who is compromised in other ways (e.g., with AIDS), severe opioid withdrawal could be fatal – for example, because of repeated vomiting.

Repeated Administration and Withdrawal

Two types of opioid withdrawal associated with mu opioid agonists:

Spontaneous withdrawal

Precipitated withdrawal

1. The opioid withdrawal syndrome can occur under two circumstances.

Repeated Administration and Withdrawal

Spontaneous Withdrawal

Occurs when a person physically dependent on mu agonist opioids suddenly stops or markedly decreases the amount of use

For heroin: usually begins 6-12 hours after last dose, peaks at 36-72 hours, and lasts about 5 days (with possible protracted withdrawal?)

1. Clinicians have noted that some patients appear to have protracted withdrawal – for example, sleep disturbance that lasts for weeks or months. However, supportive studies of a protracted opioid withdrawal syndrome are needed.

Repeated Administration and Withdrawal

Spontaneous Withdrawal (continued)

For opioids with longer half-lives (e.g., methadone), there is a longer period before onset (methadone: 36-72 hours), longer period before peak effects occur

Medications with longer half-lives generally have less severe spontaneous withdrawal syndrome

1. Methadone is an example of an opioid with a longer half-life, and its withdrawal usually begins 36-72 hours after the last dose, peaks between days 4 and 6, and lasts about 10-12 days.

Repeated Administration and Withdrawal

Precipitated Withdrawal

Occurs with administration of an opioid antagonist to a person physically dependent upon mu agonist opioids

Is qualitatively similar to spontaneous withdrawal but faster onset, and duration depends upon half life of antagonist

1. Note that the administration of an opioid antagonist to the person who is not physically dependent on opioids produces no effect.
2. There is a related note here which may be necessary to discuss if someone raises the question about acute physical dependence. In both animal and human laboratory studies, it has been shown that a single dose of an opioid agonist in a non-dependent organism, followed shortly afterwards by a very large dose of an opioid antagonist, can result in a precipitated withdrawal syndrome. This phenomenon is called acute physical dependence. It has minimal clinical relevance, although it does suggest that adaptational changes may start in people following their first use of an opioid.

Repeated Administration and Withdrawal

Precipitated Withdrawal (continued)

While the most common situation is for an antagonist such as naloxone or naltrexone to precipitate withdrawal, it is possible for a partial agonist such as buprenorphine to precipitate withdrawal under certain circumstances

A partial agonist displaces a full agonist, but only partially activates the receptor (a net decrease in activation)

Repeated Administration and Withdrawal

Precipitated Withdrawal (continued)

Withdrawal precipitated by a partial agonist is more likely if there is:

High level of physical dependence

Short time interval between administration of full agonist and partial agonist

High dose of partial agonist

1. Partial agonist-precipitated withdrawal will be reviewed in more detail later in this talk.

General Opioid Pharmacology

Opioid receptors

The functions of drugs at receptors

Repeated administration and withdrawal of opioid drugs

Affinity and dissociation

Characteristics of drugs with abuse potential

Affinity and Dissociation

Affinity:

Strength with which a drug binds to its receptor
(Strength of binding is not related to activation or efficacy at the receptor)

Dissociation:

Speed (slow or fast) of disengagement or uncoupling of drug from the receptor

1. Affinity is not the same as activation. A drug can bind with high affinity to a receptor, but not activate the receptor – an example is an opioid antagonist.

General Opioid Pharmacology

Opioid receptors

The functions of drugs at receptors

Repeated administration and withdrawal of opioid drugs

Affinity and dissociation

Characteristics of drugs with abuse potential

Characteristics of Drugs with Abuse Potential

Abuse Potential of a Drug Can Vary as a Function of:

Route of administration (faster routes such as injecting, smoking = greater abuse potential)

Half life (shorter half life = greater abuse potential)

Lipophilicity (more rapidly reaches brain = greater abuse potential)

1. These are features which can contribute to the abuse potential of a drug.

Outline for This Talk

- I. General opioid pharmacology
- II. Pharmacology of buprenorphine**
- III. Pharmacology of buprenorphine/naloxone
- IV. Summary

1. Now we're going to take these features of opioid pharmacology that have just been reviewed, and characterize buprenorphine on these different parameters.

[Reference:

Buprenorphine: Combatting Drug Abuse with a Unique Opioid. Cowan A., Lewis J.W. (eds), Wiley-Liss, New York, 1995.

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Pharmacology of Buprenorphine

Overview

Affinity and dissociation

Bioavailability

Abuse potential

Potential for physical dependence

Metabolism and excretion

1. We'll begin with an overview to buprenorphine's pharmacology.

Overview

Buprenorphine a thebaine derivative

High potency

Available as a parenteral analgesic

Produces sufficient agonist effects to be detected by the patient

Used outside United States for the treatment of opioid dependence

1. Buprenorphine is a thebaine derivative. (Thebaine is an alkaloid from opium.) This is important, because it leads to buprenorphine's legal classification as an opioid.
2. It has high potency.
3. Buprenorphine has been available for years in the United States as a parenteral analgesic. It is a safe and effective analgesic. Typical analgesic doses are 0.3-0.6 mg i.m. or i.v. every 6 (or more) hours.
4. It's important to note that buprenorphine does produce mu agonist effects (even though it is a partial mu agonist). Buprenorphine is mildly reinforcing, which means that an opioid-experienced person detects an effect with buprenorphine. (This is unlike a pure opioid antagonist, like naltrexone.) Clinically, this is desirable because it means patients are motivated to reliably maintain themselves on buprenorphine – unlike opioid antagonist maintenance.

Pharmacology of Buprenorphine

Overview

Affinity and dissociation

Bioavailability

Abuse potential

Potential for physical dependence

Metabolism and excretion

Affinity and Dissociation

Buprenorphine has:

high affinity for mu opioid receptor –

competes with other opioids and blocks their effects

slow dissociation from mu opioid receptor –

prolonged therapeutic effect for opioid dependence treatment

1. Buprenorphine has high affinity for the mu opioid receptor. This means that it is hard for other opioids with lower affinity to displace buprenorphine from the mu receptor (so it blocks their effects).
2. Buprenorphine's slow dissociation from the mu receptor results in a prolonged therapeutic effect. Considerable evidence suggests buprenorphine can be given three times per week (rather than daily), and there is some evidence suggesting buprenorphine can be given even less frequently (e.g., two times per week).
3. Buprenorphine's long duration of action when used as a medication for the treatment of opioid dependence contrasts with its relatively short analgesic effects.

Pharmacology of Buprenorphine

Overview

Affinity and dissociation

Bioavailability

Abuse potential

Potential for physical dependence

Metabolism and excretion

Bioavailability

Good parenteral bioavailability

Poor oral bioavailability

Fair sublingual bioavailability

For opioid dependence treatment:

early clinical trials used an alcohol-based solution

FDA approval for tablets that are held under tongue

1. Buprenorphine has poor oral bioavailability.
2. It is administered as tablets held under the tongue when used for the treatment of opioid dependence. Absorption of the drug is through the buccal mucosa.
3. Sublingual bioavailability is fair.
4. If you are reading about results from clinical trials, you need to consider if the study used a sublingual solution versus sublingual tablets. Several of the early clinical studies of buprenorphine for the treatment of opioid dependence used a solution form sublingually (since tablets were not yet available). There is better bioavailability for the solution versus tablets, so the doses need to be adjusted accordingly.

Bioavailability

Considerable variability between patients in bioavailability of tablets

Tablets about 50-70% bioavailable relative to solution

1. Studies of bioavailability of buprenorphine tablets and solution lead to the following conclusions:
 - a. There can be considerable variability among patients in the amount of buprenorphine absorbed from sublingual tablets
 - b. The bioavailability of the tablets is about 50-70% that of the solution
2. A common dose of buprenorphine solution used in clinical trials was 8 mg of daily sublingual solution. This would be approximately equal to 12-16 mg of sublingual tablets.

[References:

Schuh K.J., Johanson C.-E. Pharmacokinetic comparison of the buprenorphine sublingual liquid and tablet. *Drug Alcohol Depend* 56:55-60, 1999.

Nath R.P., Upton R.A., Everhart E.T., Cheung P., Shwonek P., Jones R.T., Mendelson J.E. Buprenorphine pharmacokinetics: relative bioavailability of sublingual tablet and liquid formulations. *J Clin Pharmacol* 39:619-623, 1999.]

Pharmacology of Buprenorphine

Overview

Affinity and dissociation

Bioavailability

Abuse potential

Potential for physical dependence

Metabolism and excretion

1. Next we'll review the relative abuse potential of buprenorphine.

Abuse Potential

Buprenorphine is abusable (epidemiological, human laboratory studies show)

Diversion and illicit use of analgesic form (by injection)

Relatively low abuse potential compared to other opioids

1. Epidemiological reports and human laboratory studies have shown that there can be diversion and abuse of the injectable form of buprenorphine used for analgesia. This is consistent with buprenorphine's effects at the mu opioid receptor.
2. There have been epidemiological reports from several different countries (England, Ireland, Scotland, India, New Zealand) of diversion and illicit use by injection of the analgesic form of buprenorphine.
3. Note that the abuse potential of buprenorphine is lower when compared to full agonist opioids (such as morphine and heroin).

[References:

O'Connor J.J., Moloney E., Travers R., Campbell A.: Buprenorphine abuse among opiate addicts. *Br J Addict*, 83: 1085-1087, 1988.

Singh R.A., Mattoo S.K., Malhotra A., Varma V.K.: Cases of buprenorphine abuse in India. *Acta Psychiatr Scand*, 86: 46-48, 1992.

Robinson G.M., Dukes P.D., Robinson B.J., Cooke R.R., Mahoney G.N.: The misuse of buprenorphine and a buprenorphine-naloxone combination in Wellington, New Zealand. *Drug Alcohol Depend*, 33: 81-86, 1993.]

Abuse Potential

Human laboratory studies of abuse liability in two populations:

Non-dependent opioid users

Physically dependent opioid users

1. Human laboratory studies of abuse liability of buprenorphine have tested two relevant populations: non-dependent opioid users (i.e., person who uses or has a history of use/abuse but is not physically dependent on opioids), and physically dependent opioids users. Each population will be reviewed in the following slides.

Abuse Potential

Non-dependent opioid user

Single doses of buprenorphine produce typical mu agonist effects

shown when given by injection and sublingual route

Onset of effects slower for sublingual route (suggesting lower abuse potential)

1. In non-dependent opioids users (i.e., patients who have a history of use of opioids, but are not presently physically dependent on opioids), studies have tested buprenorphine administered by injection and sublingual routes.
2. When buprenorphine is injected, the profile of effects produced – for example, pupillary constriction and mild euphoria – is similar to effects of other mu agonist opioids (e.g., morphine). This suggests buprenorphine could be abused in the same way other mu agonist opioids are abused.
3. There is a slower onset of effects when buprenorphine is taken by the sublingual route. Such slower onset suggests a lower abuse potential by this route.
4. Doses as high as 32 mg sublingual buprenorphine (solution) have been given to non-dependent opioid abusers and tolerated without adverse effect. Notably, there was no significant respiratory depression in that study. (Note this dose is equal to approximately 48-64 mg of sublingual tablets.)

[References:

Jasinski D.R., Fudala P.J., Johnson R.E.: Sublingual versus subcutaneous buprenorphine in opiate abusers. *Clin Pharmacol Ther*, 45: 513-519, 1989.

Pickworth W.B., Johnson R.E., Holicky B.A., Cone E.J.: Subjective and physiologic effects of intravenous buprenorphine in humans. *Clin Pharmacol Ther*, 53: 570-576, 1993.]

Abuse Potential

Physically dependent opioid user

Abuse potential of buprenorphine varies as function of three factors:

level of physical dependence

time interval between last dose of agonist and first dose of administered buprenorphine

dose of buprenorphine

1. We'll consider each of these factors in detail in the following slides.

[References:

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Abuse Potential

Level of physical dependence

The higher the level of physical dependence, the greater chance of precipitated withdrawal

For example:

With maintenance on 60 mg/day of methadone – precipitated withdrawal seen with single doses of sublingual buprenorphine

With maintenance on 30 mg/day methadone – markedly decreased risk of precipitated withdrawal with buprenorphine

1. If a person has a high level of physical dependence (e.g., in persons using substantial amounts of heroin on a daily basis), buprenorphine's partial agonist effect could result in a net decrease in receptor activation, so that the person who receives a single dose of buprenorphine experiences a precipitated withdrawal syndrome.
2. A high level of physical dependence can be judged by the reported amount of opioids used on a daily basis.
3. Most studies examining these relationships have used volunteers maintained on methadone. For example, patients maintained on 60 mg of daily methadone can experience precipitated withdrawal from acute doses of sublingual buprenorphine. However, in persons maintained on 30 mg of daily methadone, buprenorphine can produce either no opioid effects (i.e., neither opioid antagonist or agonist effects), opioid agonist effects (if there is a sufficient time interval between methadone and buprenorphine doses, as reviewed below), or mild opioid antagonist effects (again, if the time interval is short – as reviewed below). This suggests that at sufficient time intervals, buprenorphine can be safely given to patients with relatively low levels of physical dependence (equivalent to 30 mg of daily oral methadone), with low risk of precipitated withdrawal.

Abuse Potential

Time interval

At short time intervals (e.g., 2 hours after a dose of methadone), increased likelihood of buprenorphine precipitated withdrawal

At longer time intervals, more likely buprenorphine is either placebo-like or opioid agonist-like

1. If there is a relatively short time interval between the last dose of agonist and first dose of buprenorphine, then there is a greater likelihood of precipitated withdrawal.
2. For example, in subjects maintained on 30 mg of daily methadone (a low level of physical dependence), no precipitated withdrawal is seen when 20 hours elapse between the dose of methadone and the dose of buprenorphine. However, at 2 hours between the methadone dose and buprenorphine administration, precipitated withdrawal is seen.
3. At longer time intervals, it is more likely buprenorphine is either placebo-like or opioid agonist-like.
4. The precipitated withdrawal seen with buprenorphine is mild in intensity.

Abuse Potential

Dose of buprenorphine

Low single doses of buprenorphine given acutely produce minimal effects (e.g., placebo-like or opioid agonist-like)

Higher doses can precipitate withdrawal in persons physically dependent on opioids

1. Low doses of injected buprenorphine (e.g., 2 mg) tend to produce no effects – they are neither agonist-like nor antagonist-like. They are usually identified as placebo.
2. Higher doses of buprenorphine at longer time intervals (20+ hours) and lower levels of physical dependence (the equivalent of 30 mg of methadone per day) are more likely to be identified as opioid agonist-like.
3. At shorter time intervals and with higher levels of physical dependence, higher doses of buprenorphine are more likely to precipitate withdrawal.

Pharmacology of Buprenorphine

Overview

Affinity and dissociation

Bioavailability

Abuse potential

Potential for physical dependence

Metabolism and excretion

Potential for Physical Dependence

Repeated administration of buprenorphine produces or maintains physical dependence

However, degree of physical dependence is less than that produced by full agonist opioids

This means withdrawal syndrome should be less severe for buprenorphine

1. Because buprenorphine is a partial agonist, the degree of physical dependence is less than that seen for full agonists.
2. Thus, for example, administration of an opioid antagonist to a buprenorphine-maintained person produces a mild withdrawal syndrome.

[Reference:

Eissenberg T., Greenwald M.K., Johnson R.E., Liebson I.A., Bigelow G.E., Stitzer M.L. Buprenorphine's physical dependence potential: antagonist-precipitated withdrawal in humans. *J Pharmacol Exp Ther* 276:449-459, 1996.]

Pharmacology of Buprenorphine

Overview

Affinity and dissociation

Bioavailability

Abuse potential

Potential for physical dependence

Metabolism and excretion

Metabolism and Excretion

High percentage of buprenorphine bound to plasma protein

Metabolized in liver by cytochrome P450 3A4 enzyme system into norbuprenorphine and other metabolites

[References:

Iribarne C., Picart D., Dréano Y., Bail J.-P., Berthou F. Involvement of cytochrome P450 3A4 in *N*-dealkylation of buprenorphine in human liver microsomes. *Life Sciences* 60:1953-1964, 1997.

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Outline for This Talk

- I. General opioid pharmacology
- II. Pharmacology of buprenorphine
- III. Pharmacology of buprenorphine/naloxone**
- IV. Summary

1. While the focus of this talk has been on buprenorphine, a combination of buprenorphine with naloxone (in a tablet form) has been developed, and it is likely that this form will be used for maintenance treatment in opioid dependence.
2. The reason for combining buprenorphine with naloxone is to decrease the potential abuse of buprenorphine. Sublingual tablets of buprenorphine need to be water soluble, so it is possible a person would dissolve a tablet and then inject it if the tablet contained buprenorphine alone. However, if a person physically dependent on an opioid such as heroin dissolved and injected a tablet containing buprenorphine combined with naloxone, he/she would experience a predominant naloxone effect – i.e., a precipitated withdrawal syndrome.

Pharmacology of Buprenorphine/Naloxone

Sublingual naloxone

Combination of naloxone plus buprenorphine

Diversion and misuse of buprenorphine/naloxone

Sublingual Naloxone

Sublingual naloxone has relatively poor bioavailability

Dose up to 1-2 mg sublingual do not precipitate withdrawal
in opioid dependent volunteers

Sublingual naloxone does have a bitter taste

1. Sublingual naloxone has relatively poor bioavailability – especially for doses of up to 2 mg.
2. Sublingual naloxone does have a bitter taste – for this reason, tablets containing naloxone also contain a flavoring agent.

[Reference:

Preston K.L., Bigelow G.E., Liebson I.A. Effects of sublingually given naloxone in opioid-dependent human volunteers. *Drug Alcohol Depend* 25:27-34, 1990.]

Pharmacology of Buprenorphine/Naloxone

Sublingual naloxone

Combination of naloxone plus buprenorphine

Diversion and misuse of buprenorphine/naloxone

Combination of Buprenorphine plus Naloxone

Sublingual buprenorphine has fair bioavailability

Addition of naloxone to buprenorphine to decrease abuse potential of tablets

Combination ratio is 4 to 1 (buprenorphine to naloxone)

1. There are two tablet sizes:

small (containing 2 mg of buprenorphine combined with 0.5 mg of naloxone), and

large (containing 8 mg of buprenorphine combined with 2 mg of naloxone)

2. In addition, corresponding tablets of buprenorphine alone (2 and 8 mg, for dose induction purposes) should be available.

Combination of Buprenorphine plus Naloxone

Combination tablet containing buprenorphine with naloxone
– if taken under tongue, predominant buprenorphine effect

If opioid dependent person dissolves and injects
buprenorphine/naloxone tablet – predominant naloxone effect (and precipitated withdrawal)

References:

Fudala P.J, Yu E, Macfadden W., Boardman C., Chiang C.N. Effects of buprenorphine and naloxone in morphine-stabilized opioid addicts. *Drug Alcohol Depend* 50:1-8, 1998.

Mendelson J., Jones R.T., Fernandez I., Welm S., Melby A.K., Baggott M.J. Buprenorphine and naloxone interactions in opiate-dependent volunteers. *Clin Pharmacol Ther* 60:105-114, 1996.

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Pharmacology of Buprenorphine/Naloxone

Sublingual naloxone

Combination of naloxone plus buprenorphine

Diversion and misuse of buprenorphine/naloxone

Diversion and Misuse

Four possible groups that might attempt to divert and parenterally abuse buprenorphine/naloxone:

1. Persons physically dependent on illicit opioids
2. Persons on prescribed opioids (e.g., methadone)
3. Persons maintained on buprenorphine/naloxone
4. Persons abusing, but not physically dependent on opioids

1. Note there are four possible groups that might attempt to parenterally abuse buprenorphine/naloxone.
2. For persons physically dependent on an illicit agonist opioid (like heroin), injection of buprenorphine/naloxone will precipitate withdrawal (or, if the dose is very low – e.g., 1/0.25 mg – it will produce placebo-like effects).
3. For persons physically dependent on a prescribed opioid (like methadone or LAAM), injection of buprenorphine/naloxone will precipitate withdrawal (or, again, if the dose is very low it will produce placebo-like effects).
4. For persons maintained on sublingual buprenorphine/naloxone, injection of buprenorphine/naloxone could produce opioid agonist effects (with no precipitated withdrawal from the naloxone, since high doses of naloxone are needed to precipitate withdrawal in buprenorphine maintained persons). Note that this is a population that will have access and may be very likely to dissolve and inject buprenorphine/naloxone tablets, since they will have a ready supply of them.
5. For persons not physically dependent on opioids, naloxone will not precipitate withdrawal and it is likely the buprenorphine will produce opioid agonist effects.

Diversion and Misuse

The sublingual form of buprenorphine/naloxone combination might be diverted

1. In addition to parenteral use/abuse of buprenorphine/naloxone, this combination could be abused sublingually. There are two possible groups that might use/abuse the sublingual form of buprenorphine/naloxone: persons physically dependent on opioids, and persons not physically dependent on opioids. Abuse may be more likely in the latter group.
2. However, abuse of buprenorphine/naloxone by the sublingual route is less likely, since the onset of effects is slower and the magnitude of effects is less. There might be some abuse of tablets sublingually – for example, in persons who are early in their opioid abuse history and are not injecting drugs. Recall that buprenorphine has agonist effects and is mildly reinforcing.
3. Similarly, it is possible that tablets might be used sublingually for experimentation by persons without a history of opioid abuse.

Outline for This Talk

- I. General opioid pharmacology
- II. Pharmacology of buprenorphine
- III. Pharmacology of buprenorphine/naloxone
- IV. Summary

Summary

Buprenorphine a partial mu agonist opioid

Profile of effects similar to other mu agonist opioids, but
less risk of respiratory depression, lower level of physical
dependence

Can be abused, but combination with naloxone decreases
abuse potential

Applied Pharmacology

Applied Pharmacology

Outline for This Talk

- I. Efficacy of buprenorphine
- II. Safety of buprenorphine
- III. Clinical use of buprenorphine
- IV. Summary

Outline for This Talk

- I. Efficacy of buprenorphine
- II. Safety of buprenorphine
- III. Clinical use of buprenorphine
- IV. Summary

1. The remainder of this talk will focus on clinical aspects of buprenorphine's use in the treatment of opioid dependence.

Efficacy of Buprenorphine

Maintenance treatment using buprenorphine

Medically-managed withdrawal using buprenorphine

1. First we'll begin by addressing the efficacy of buprenorphine for each of these clinical situations – maintenance and withdrawal.

Maintenance Treatment Using Buprenorphine

Numerous outpatient clinical trials comparing efficacy of daily buprenorphine to placebo, and to methadone.

1. Note most studies of buprenorphine's efficacy tested daily buprenorphine to daily methadone or to placebo. Most studies have been conducted in traditional methadone clinic settings (i.e, patients attend the clinic daily and receive supervised medication).
2. Primary outcome measures from these studies have typically been treatment retention and urinalysis results.
3. Compliance has been good in taking buprenorphine (consistent with the mildly reinforcing properties of a mu partial agonist opioid).

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Maintenance Treatment Using Buprenorphine

These studies conclude:

Buprenorphine more effective than placebo

Buprenorphine equally effective as moderate doses of methadone (e.g., 60 mg per day)

1. In general, these studies have shown buprenorphine and methadone are equivalent on primary outcome measures (treatment retention, rates of positive urine samples for illicit opioids).
2. It is not clear if buprenorphine can be as effective as higher doses of methadone (e.g., 80-100+ mg per day), and therefore may not be the treatment of choice for patients with higher levels of physical dependence. This may be related to buprenorphine's partial agonist effects – that is, higher doses of methadone continue to exert increasing effects, but higher doses of buprenorphine reach a plateau in their effectiveness.
3. Buprenorphine appears to be equally effective as moderate doses of LAAM, too.

Efficacy of Buprenorphine

Maintenance treatment using buprenorphine

Medically-managed withdrawal using
buprenorphine

Withdrawal Using Buprenorphine

Studies have primarily looked at buprenorphine maintenance, not withdrawal

In general, withdrawal using opioids (e.g., methadone) has had poor outcomes

Results with buprenorphine may be better (may have a milder withdrawal syndrome)

1. While there are several controlled clinical trials that have tested the efficacy of buprenorphine maintenance, there has been little systematic work testing buprenorphine for opioid withdrawal.
2. Studies of methadone withdrawal have generally shown poor outcomes (as measured by relapse to opioid use). However, it is interesting to note that illicit opioid use appears to be lowered by an episode of methadone treatment, even if complete abstinence is not initiated or maintained. It is not clear if this effect is unique to methadone treatment, or may be seen with other medications (such as buprenorphine).
3. Buprenorphine is thought to have a milder withdrawal syndrome when compared to full agonist opioids like methadone. This milder withdrawal syndrome may make it a better medication for use in opioid withdrawal.

[References:

Cheskin L.J., Fudala P.J., Johnson R.E. A controlled comparison of buprenorphine and clonidine for acute detoxification from opioids. *Drug Alcohol Depend* 36:115-121, 1994.

Nigam A.K., Ray R., Tripathi B.M. Buprenorphine in opiate withdrawal: a comparison with clonidine. *J Subst Abuse Treatment* 10: 391-394, 1993.

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Outline for This Talk

- I. Efficacy of buprenorphine
- II. **Safety of buprenorphine**
- III. Clinical use of buprenorphine
- IV. Summary

Safety of Buprenorphine

Overview

Teratogenesis

Precipitated withdrawal

Overdose

Drug interactions

1. These features related to safety will be considered in turn.
2. We'll begin with some general points regarding buprenorphine's safety.

References:

Johnson R.E., Jaffe J.H., Fudala P.J. A controlled trial of buprenorphine treatment for opioid dependence. *JAMA* 267:2750-2755, 1992.

Lange, W.R., Fudala, P.J., Dax, E.M., and Johnson, R.E. Safety and side-effects of buprenorphine in the clinical management of heroin addiction. *Drug Alcohol Depend.* 26, 19-28, 1990.

Ling W., Charuvastra C., Collins J.F., Batki S., Brown L.S., Kintaudi P., Wesson D.R., McNicholas L., Tusel D.J., Malkerneker U., Renner J.A., Santos E., Casadonte P., Fye C., Stine S., Wang R.I.H., Segal D. Buprenorphine maintenance treatment of opiate dependence: A multicenter, randomized clinical trial. *Addiction* 93:475-486, 1998.]

Overview to Safety

Highly safe medication (acute and chronic dosing)

Primary side effects: like other mu agonist opioids (e.g., nausea, constipation), but may be less severe

No evidence of significant disruption in cognitive or psychomotor performance with buprenorphine maintenance

No evidence of organ damage with chronic dosing

1. Buprenorphine is a highly safe medication for use in patients with opioid dependence.
2. Note that it is also safe if inadvertently taken by a person who is not physically dependent on opioids (such as a child). In such a case, it is most likely the person would swallow the tablet and experience virtually no opioid agonist effect because of the poor oral bioavailability. Even if the person sucked on the tablet, there is a low likelihood that they would experience serious adverse effects. This is because buprenorphine is a partial opioid agonist, and there is a ceiling in the maximal effects produced.
3. Clinical trials with buprenorphine have found no significant organ damage associated with chronic dosing. However, buprenorphine may be associated with increases in liver function tests, and this may be especially true for patients with a history of hepatitis prior to the onset of buprenorphine treatment. Increases in liver function tests appear to be mild, and it is important to keep in mind that other factors commonly found in opioid dependent patients (such as hepatitis and alcohol abuse) can lead to elevations in liver function tests.

[References:

Petry, N. M., Bickel, W. K., Piasecki, D., Marsch, L. A., Badger, G. J. Elevated liver enzyme levels in opioid-dependent patients with hepatitis treated with buprenorphine. *Am J Addict* 9:265-9, 2000.

Lange W.R., Fudala P.J., Dax E.M., Johnson R.E. Safety and side-effects of buprenorphine in the clinical management of heroin addiction. *Drug Alcohol Depend* 26:19-28, 1990.]

Safety of Buprenorphine

Overview

Teratogenesis

Precipitated withdrawal

Overdose

Drug interactions

Teratogenesis

Limited information about use of buprenorphine in pregnant, opioid dependent women

No reports of teratogenic effects (but limited number of cases)

Review of buprenorphine use in pregnancy in Special Populations lecture

1. Available data about use of buprenorphine in pregnant, opioid dependent women has been primarily limited to case reports.
2. There have not been any reports on significant problems attributed to buprenorphine use during pregnancy.

[Reference:

Fischer, G., Johnson, R.E., Eder, H., Yagsch, R., Peternell, A., Wehinger, M., Langer, M., Aschauer H.N. Treatment of opioid-dependent pregnant women with buprenorphine. *Addiction* 95:239-244, 2000.]

Safety of Buprenorphine

Overview

Teratogenesis

Precipitated withdrawal

Overdose

Drug interactions

Precipitated Withdrawal

Reviewed in Basic Pharmacology section

Buprenorphine-precipitated withdrawal seen in controlled studies has been mild in intensity and of short duration

1. The potential for buprenorphine-precipitated withdrawal has been covered elsewhere in the Basic Pharmacology section, and will not be reviewed in detail here.
2. While it is possible for buprenorphine to precipitate withdrawal during buprenorphine induction, and this possibility has received significant attention and review in this curriculum, it is important to keep this potential in perspective. The likelihood for buprenorphine-precipitated withdrawal is low, and even when it does occur, it is mild in intensity and short in duration. The clinician should be aware of the potential, but not allow the potential to deter from use of buprenorphine.

Safety of Buprenorphine

Overview

Teratogenesis

Precipitated withdrawal

Overdose

Drug interactions

Overdose with Buprenorphine

Low risk of clinically significant problems

No reports of respiratory depression in clinical trials comparing buprenorphine to methadone

Pre-clinical studies suggest high doses of buprenorphine should not produce respiratory depression or other significant problems

Overdose of buprenorphine combined with other drugs may cause problems (reviewed below)

1. The risk of developing clinically significant problems from a buprenorphine overdose is low. Unlike full agonist opioids (such as methadone and heroin), the maximal opioid agonist effect produced by buprenorphine – a partial agonist – is relatively low. The maximal effects of buprenorphine appear to occur in the 8-16 mg dose range for sublingual solution (in non-dependent opioid abusers). This is equal to 16-32 mg of sublingual tablets. This means that higher doses are unlikely to produce greater effects (and may actually produce less effects, based on pre-clinical evidence).

2. This ceiling on the effects produced means buprenorphine is less likely to produce clinically significant respiratory depression. However, overdose in situations where buprenorphine is combined with other CNS depressants may be fatal, as reviewed later in this section.

[Reference:

Walsh S. L., Preston K.L., Stitzer M.L., Cone E.J., Bigelow G.E. Clinical pharmacology of buprenorphine: ceiling effects at high doses. Clin Pharmacol Ther 55:569-80, 1994.]

Safety of Buprenorphine

Overview

Teratogenesis

Precipitated withdrawal

Overdose

Drug interactions

Drug Interactions with Buprenorphine

Benzodiazepines and other sedating drugs

Medications metabolized by cytochrome P450 3A4

Opioid antagonists

Opioid agonists

Benzodiazepines and Other Sedating Drugs

Reports of deaths when buprenorphine injected along with benzodiazepines

Reported from France, where tablets available – appears patients dissolve and inject tablets

Probably possible for this to occur with other sedatives as well

1. It is not clear, based upon the French experience with buprenorphine-related deaths, if any patients have died from use of sublingual buprenorphine combined with oral benzodiazepine. It appears likely that most deaths have been related to injection of the combination of dissolved buprenorphine tablets with benzodiazepine.
2. Note that the combination product (buprenorphine with naloxone) is designed to decrease the likelihood that people will dissolve and inject buprenorphine.
3. The mechanism leading to death in these cases is not known.

[References:

Reynaud M., Tracqui A., Petit G., Potard D., Courty P. Six deaths linked to misuse of buprenorphine-benzodiazepine combinations. *Am. J. Psychiatry* 155, 448-449, 1998.

Tracqui A., Kintz P., Ludes B. Buprenorphine-related deaths among drug addicts in France: A report on 20 fatalities. *J. Analytic. Tox.* 22, 430-434, 1998.

Gaulier J. M., Marquet P., Lacassie E., Dupuy J. L., Lachatre G. Fatal intoxication following self-administration of a massive dose of buprenorphine. *J Forensic Sci* 45:226-8, 2000.]

Drug Interactions with Buprenorphine

Benzodiazepines and other sedating drugs

Medications metabolized by cytochrome P450 3A4

Opioid antagonists

Opioid agonists

1. Recall that buprenorphine is metabolized by the cytochrome P450 3A4 enzyme system, and therefore has the potential to affect and be affected by other medications that use the same enzyme system.
2. Drug interactions for the P450 system can be checked at the web site:
www.drug-interactions.com

Medications Metabolized by P450 3A4

Examples of other medications that interact with the cytochrome P450 3A4 enzyme system are:

Nifedipine

Erythromycin

HIV protease inhibitors (e.g., Ritonavir)

Note no controlled studies have directly examined these possible interactions

1. There are numerous medications that interact with the P450 3A4 enzyme system – either as inhibitors, inducers, or substrates. This is only a limited list. A more extensive list can be found in the Buprenorphine Guidelines document (and as www.drug-interactions.com).

Medications Metabolized by P450 3A4

Other categories of medications that interact with the cytochrome P450 3A4 enzyme system are:

- Oral contraceptives
- Certain anticonvulsants
- Certain antidepressants

1. Included in these other medications that interact with the 3A4 system are oral contraceptives, several common anticonvulsants (e.g., phenytoin, carbamazepine, phenobarbital), antidepressants (e.g., paroxetine, nefazadone, certain tricyclic antidepressants), and grapefruit juice.

Drug Interactions with Buprenorphine

Benzodiazepines and other sedating drugs

Medications metabolized by cytochrome P450 3A4

Opioid antagonists

Opioid agonists

Opioid Antagonists

Combination tablet containing buprenorphine/naloxone is safe and indicated

But, avoid prescribing buprenorphine with an opioid antagonist such as naltrexone – for example, in a patient with combined opioid and alcohol dependence

While buprenorphine has low level of physical dependence, it may be possible to precipitate withdrawal with opioid antagonist in buprenorphine-maintained patients

1. The marketed product that combines buprenorphine with naloxone is indicated and safe to prescribe (since naloxone has poor sublingual bioavailability, as reviewed in the Basic Pharmacology section).
2. The opioid antagonist naltrexone (ReVia) is approved for the treatment of alcohol dependence – it can be a useful medication for some patients with alcoholism. However, buprenorphine should not be combined with an opioid antagonist such as naltrexone (for example, when treating a patient with combined opioid and alcohol dependence). This is because naltrexone has good oral bioavailability, and could potentially precipitate a withdrawal syndrome in a buprenorphine-maintained patient. Typical doses of naltrexone (25-50 mg p.o. as a first dose) could be sufficient to produce a precipitated withdrawal syndrome in such patients.

Drug Interactions with Buprenorphine

Benzodiazepines and other sedating drugs

Medications metabolized by cytochrome P450 3A4

Opioid antagonists

Opioid agonists

Opioid Agonists

The combination of an opioid agonist with buprenorphine should be viewed as a possible contraindication

Use caution if combining an opioid agonist (for example, morphine for pain relief) with buprenorphine – possible that buprenorphine could precipitate withdrawal under certain circumstances

1. Possible to have a clinical situation where there is a need for pain relief that requires an opioid agonist.
2. To minimize risk of precipitated withdrawal, should ensure there is an adequate time interval between dose of agonist and maintenance dose of buprenorphine.

Outline for This Talk

- I. Efficacy of buprenorphine
- II. Safety of buprenorphine
- III. Clinical use of buprenorphine
- IV. Summary

1. We'll now review the clinical use of buprenorphine in the treatment of opioid dependence.

Clinical Use of Buprenorphine

Induction

Stabilization/maintenance

Withdrawal

1. This section will review use of buprenorphine when starting medication (induction), during the maintenance phase and during withdrawal.

[Reference:

Johnson, R.E., Cone, E.J., Henningfield, J.E., Fudala, P.J. Use of buprenorphine in the treatment of opiate addiction. I. Physiologic and behavioral effects during a rapid dose induction. Clin. Pharmacol. Ther. 46, 335-343, 1989.]

Buprenorphine Induction

Patients who are not physically dependent on
opioids: Days 1, 2+

Patients dependent on short-acting opioids (e.g., heroin):

Day 1

Patients dependent on long-acting opioids (e.g.,
methadone): Day 1

Patients dependent on short- or long-acting opioids: Days
2+

1. The first group of patients that may require induction on buprenorphine are persons who have a history of opioid abuse, but are not currently showing physical dependence on opioids. The following slides provide information about buprenorphine induction for the first day, then the subsequent days.

Buprenorphine Induction

Patients not physically dependent on opioids

For example, patient at high risk for relapse to opioid use

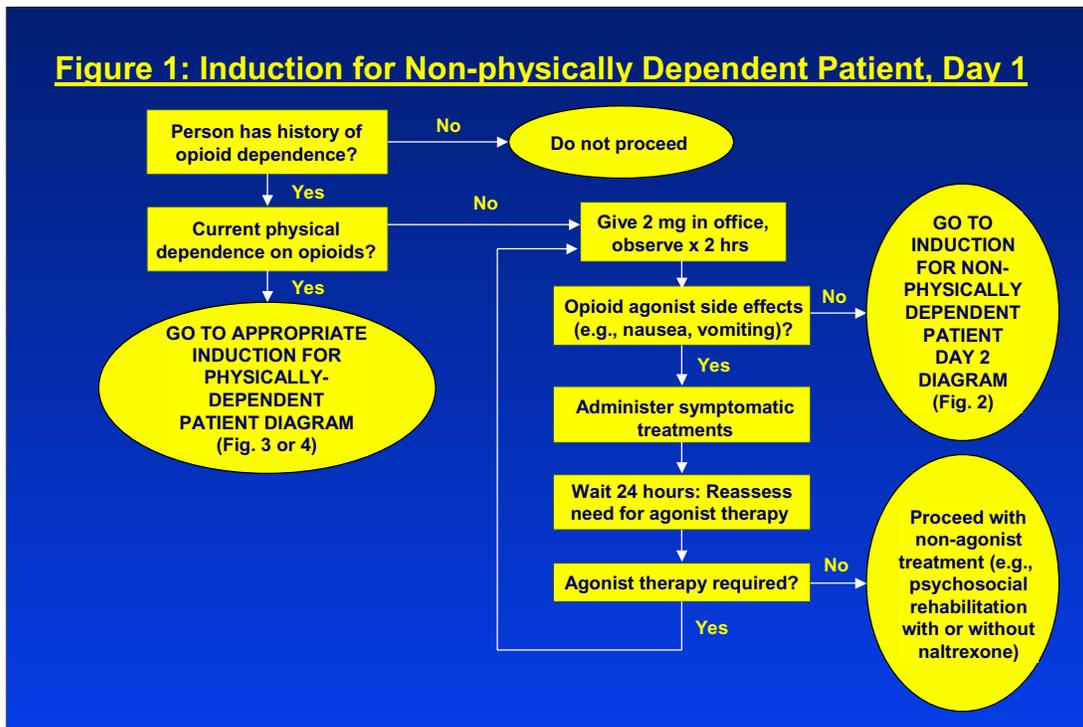
First dose: 2 mg sublingual buprenorphine

Monitor in office for 2+ hours after first dose

Gradually increase dose over days

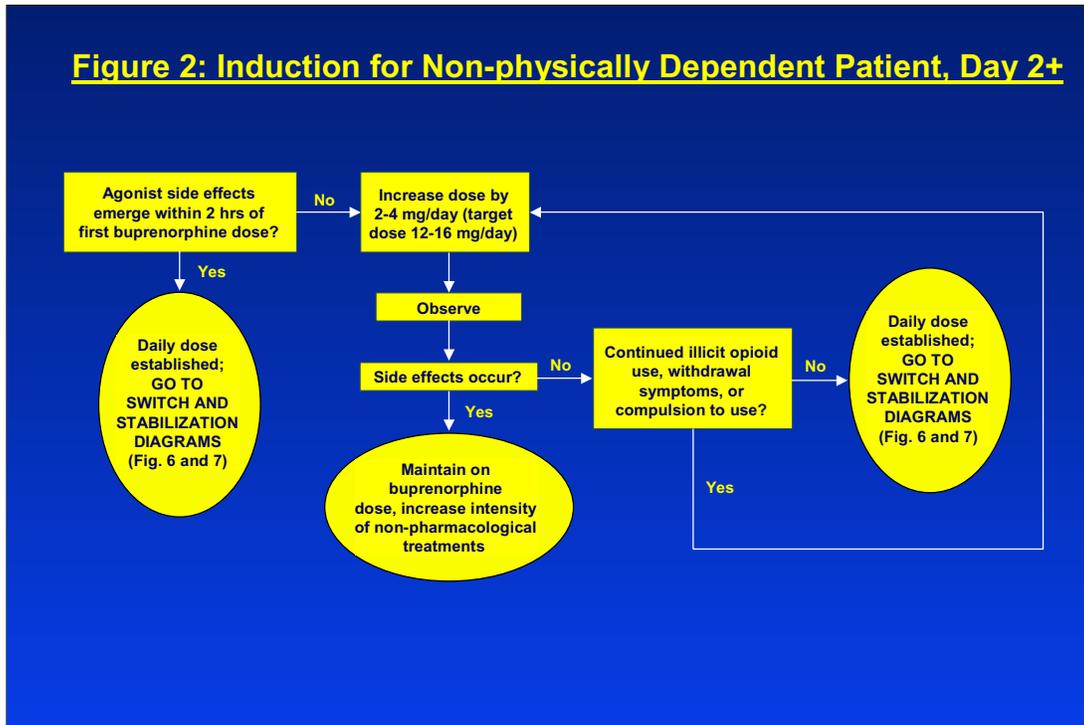
1. An example of such a patient is a person who was incarcerated, recently released, and thought to be at high risk for relapse to illicit opioid use.
2. Since such a person is not physically dependent on opioids, dose induction should be more gradual (to avoid excessive opioid agonist effect in a non-tolerant person).

Figure 1: Induction for Non-physically Dependent Patient, Day 1



1. On the first day, the patient should receive a single, 2 mg dose of buprenorphine monotherapy medication. The patient should then be monitored in the office. Assess for evidence of excessive opioid agonist effects and, if seen, treat these symptomatically. If the patient has a strong opioid agonist effect, then the daily maintenance dose may be only 2 mg (or they may not be suitable for buprenorphine maintenance treatment).

Figure 2: Induction for Non-physically Dependent Patient, Day 2+



1. On the second day, the response to the first day's dose should guide subsequent dosing. The dose can be increased by 2-4 mg each day, until targeted outcomes are achieved.

Buprenorphine Induction

Patients who are not physically dependent on opioids:

Days 1, 2+

Patients dependent on short-acting opioids (e.g., heroin): Day 1

Patients dependent on long-acting opioids (e.g., methadone): Day 1

Patients dependent on short- or long-acting opioids: Days 2+

1. Next will be a review of the first day of induction for patients dependent on short-acting opioids (e.g., heroin). Since the management of patients dependent on short- or long-acting opioids (such as methadone) is similar after the first day, treatment after the first day is reviewed later in this section.

Buprenorphine Induction

Patients dependent on short-acting opioids

Instruct patient to abstain from any opioid use for 12-24 hours (so they are in mild withdrawal at time of first buprenorphine dose)

If patient is not in opioid withdrawal at time of arrival in office, then assess time of last use and consider either having him/her return another day or wait in the office until evidence of withdrawal seen

Buprenorphine Induction

Patients dependent on short-acting opioids (continued)

First dose: 2-4 mg sublingual buprenorphine

Monitor in office for 2+ hours after first dose

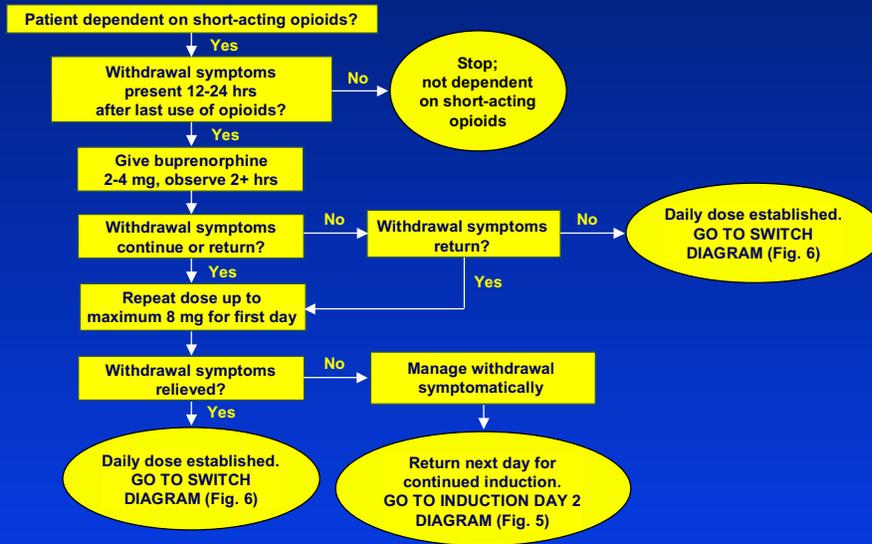
Can re-dose if needed (every 2-4 hours, if opioid withdrawal subsides then reappears)

Maximum first day dose of 8 mg

1. If opioid withdrawal appears shortly after the dose of buprenorphine, it suggests that the buprenorphine may have precipitated a withdrawal syndrome. Management of the patient can then follow one of two paths. You could give another dose of buprenorphine, attempting to provide enough agonist effect from buprenorphine to suppress the withdrawal. Or, you could stop the induction and have the patient return the next day.

Since the latter would risk loss of the patient, the first option should be considered.

Figure 3: Induction for Patient Physically Dependent On Short-acting Opioids, Day 1



Buprenorphine Induction

Patients dependent on short-acting opioids (continued)

Best to begin with buprenorphine monotherapy tablets (i.e., without naloxone) for first 2-3 days, then switch to buprenorphine/naloxone combination tablets

When switching to combination tablets, do direct switch to same dose of buprenorphine (i.e., from 8 mg daily go to 8/2 mg daily)

1. It should be stressed that induction with combination tablets is best avoided.

Buprenorphine Induction

Patients dependent on short-acting opioids (continued)

If starting with combination tablets directly, use low doses (2 mg of naloxone total), monitor longer, be more cautious with extra doses on first 1-3 days (but not recommended to start directly with combination tablets)

1.

Buprenorphine Induction

Patients who are not physically dependent on opioids:

Days 1, 2+

Patients dependent on short-acting opioids (e.g., heroin):

Day 1

**Patients dependent on long-acting opioids (e.g.,
methadone): Day 1**

Patients dependent on short- or long-acting opioids: Days

2+

1. Another group of patients who may seek office-based buprenorphine treatment are those physically dependent on long acting opioids, such as methadone or LAAM.

Buprenorphine Induction

Patients dependent on long-acting opioids

Patient should have dose decreases until on 30 mg of methadone or the equivalent

Begin induction 24 hours after last dose of methadone, 48 hours after last dose of LAAM

Give no further methadone or LAAM once buprenorphine induction is started

1. 30 mg of methadone is approximately equivalent to 35-40 mg of LAAM.
2. Patients do not need to be kept on methadone or LAAM during their induction onto buprenorphine, and should not receive any further doses of methadone or LAAM after their first buprenorphine dose.

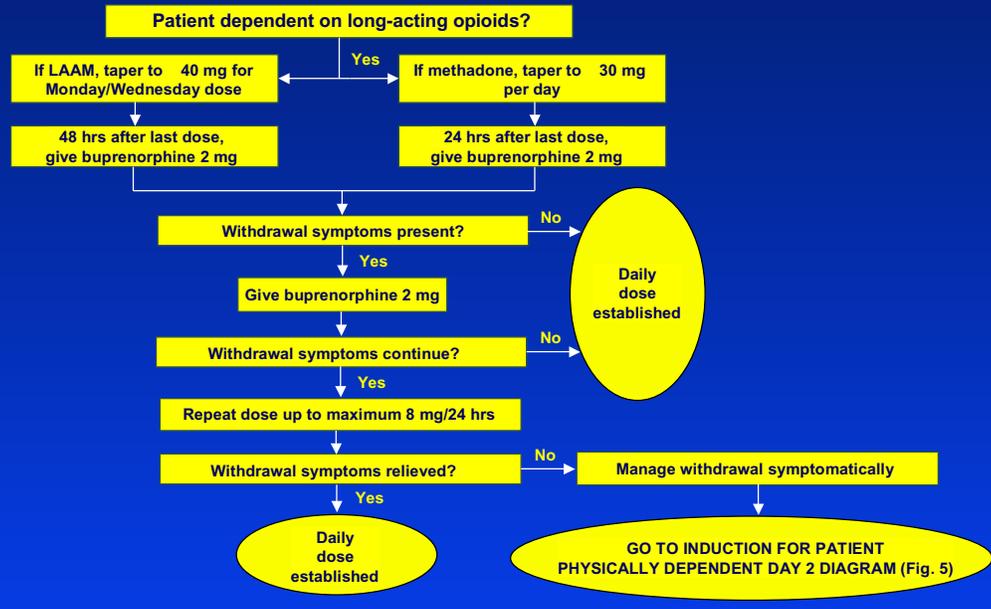
Buprenorphine Induction

Patients dependent on long-acting opioids (continued)

Use similar procedure as that described for short acting opioids

Expect total first day dose of 8 mg sublingual buprenorphine

Figure 4: Induction for Patient Physically Dependent On Long-acting Opioids, Day 1



Buprenorphine Induction

Patients who are not physically dependent on opioids:

Days 1, 2+

Patients dependent on short-acting opioids (e.g., heroin):

Day 1

Patients dependent on long-acting opioids (e.g.,
methadone): Day 1

**Patients dependent on short- or long-acting
opioids: Days 2+**

1. After the first day of buprenorphine induction for patients who are either dependent on short-acting or long acting opioids, the procedures are essentially the same.

Buprenorphine Induction

Patients dependent on short- or long-acting opioids

On second day, have patient return to the office for assessment, second day dosing

Adjust dose accordingly based on patient's experiences on first day (i.e., higher dose if there were withdrawal symptoms after leaving your office; lower dose if patient was over-medicated at end of first day)

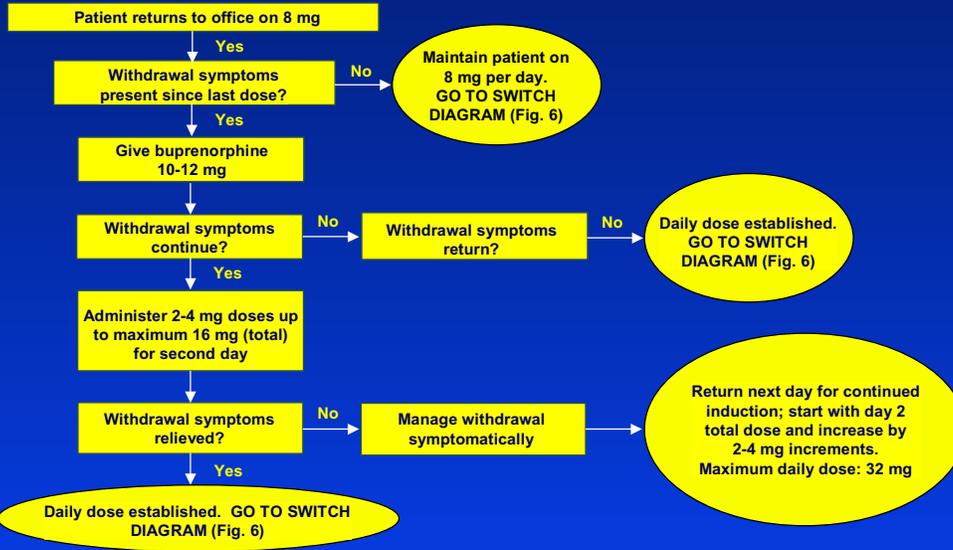
Buprenorphine Induction

Patients dependent on short- or long-acting opioids (continued)

Continue adjusting dose by 2-4 mg increments until an initial target dose of 12-16 mg is achieved for the second day

If continued dose increases are indicated after the second day, have the patient return for further dose induction (with a maximum daily dose of 32 mg)

Figure 5: Induction for Patient Physically Dependent On Short- or Long-acting Opioids, Days 2+

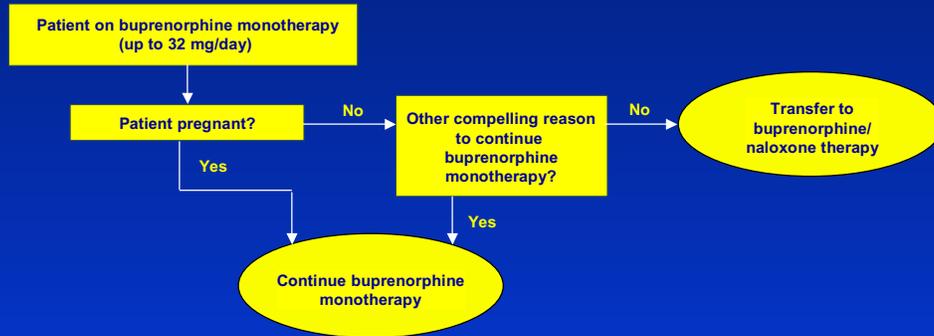


Buprenorphine Induction

Conversion to buprenorphine/naloxone

If indicated, switch patient to buprenorphine/naloxone combination tablets after 2-3 days of buprenorphine monotherapy dosing

Figure 6: Switch from Buprenorphine to Buprenorphine/naloxone



1. The conversion from buprenorphine to buprenorphine/naloxone can be done by simply switching the patient from the daily dose of buprenorphine monotherapy (e.g., 16 mg) to the corresponding daily dose of buprenorphine/naloxone combination therapy (16/4 mg).

Clinical Use of Buprenorphine

Induction

Stabilization/maintenance

Withdrawal

Buprenorphine Stabilization/maintenance

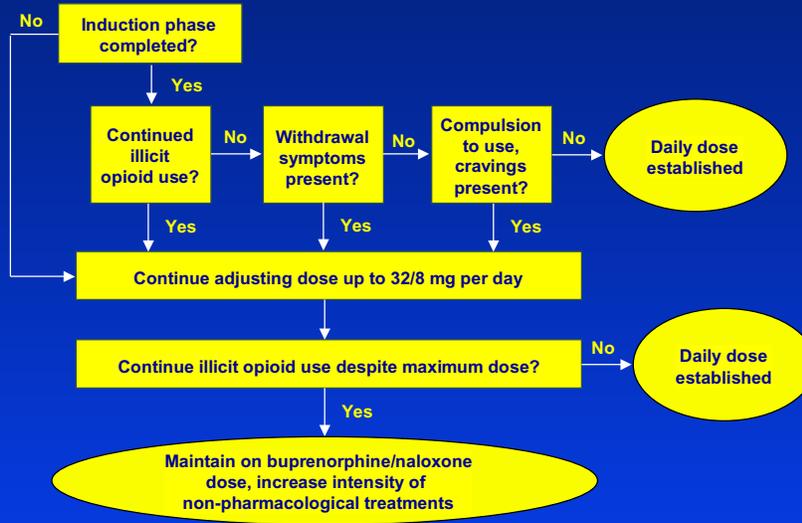
Stabilize on daily sublingual dose

Expect average daily dose will be somewhere between 8/2 and 32/8 mg of buprenorphine/naloxone

Higher daily doses more tolerable if taken sequentially rather than all at once

1. A daily dose of 32 mg will require a patient to take 4 large tablets. Tablets take about 5+ minutes to dissolve, and taking multiple tablets at once can result in a paste-like mass in the oral cavity (and poor absorption). For this reason, patients should be instructed to take tablets separately (and can space them out).
2. They may also find it helpful to sip some water before taking the tablet, to moisten their mouth.

Figure 7: Stabilization/maintenance



Buprenorphine Stabilization/maintenance

The patient should receive a daily dose until stabilized

Once stabilized, the patient can shift to alternate day dosing (e.g., every other day, MWF, may be possible to do MTh)

Increase dose on dosing day by amount not received on intervening days (e.g., if on 8 mg daily, switch to 16/16/24 mg on MWF)

1. Studies of alternate buprenorphine schedules have shown these to be well tolerated and safe.
2. Alternate day dosing should not be used until the patient has achieved stabilization on a daily dose.

[Reference:

Amass, L., Bickel, W.K., Crean, J.P., Blake, J., Higgins, S.T. Alternate-day buprenorphine dosing is preferred to daily dosing by opiate-dependent humans. *Psychopharmacology*. 136, 217-225, 1998.

Amass, L., Bickel, W.K., Higgins, S.T., Badger, G.J. Alternate-day dosing during buprenorphine treatment of opiate dependence. *Life Sci*. 54, 1215-1228, 1994a.

Amass, L., Kamien, J.B., Mikulich, S.K. Efficacy of daily and alternate-day dosing regimens with the combination buprenorphine-naloxone tablet. *Drug Alcohol Depend*. 58, 143-152, 2000.

Bickel, W.K., Amass, L., Crean, J.P., Badger, G.J. Buprenorphine dosing every 1, 2, or 3 days in opioid-dependent patients. *Psychopharmacology*, 146, 111-118, 1999.

Fudala, P.J., Jaffe, J.H., Dax, E.M., Johnson, R.E. Use of buprenorphine in the treatment of opiate addiction: II. Physiologic and behavioral effects of daily and alternate-day administration and abrupt withdrawal. *Clin. Pharmacol. Ther.* 47, 525-534, 1990.

Johnson, R.E., Eissenberg, T., Stitzer, M.L., Strain, E.C., Liebson, I.A., Bigelow, G.E. Buprenorphine treatment of opiate dependence: Clinical trial of daily versus alternate-day dosing. *Drug Alcohol Depend*. 40, 27-35, 1995b.]

Clinical Use of Buprenorphine

Induction

Stabilization/maintenance

Withdrawal

Withdrawal Using Buprenorphine

Withdrawal in 3 days (rapid)

Withdrawal over 4 to 30 days (moderate period)

Withdrawal over more than 30 days (long term)

1. There have been numerous reports of buprenorphine use for withdrawal from opioids (or “detoxification,” although this is technically not buprenorphine detoxification since buprenorphine should not be thought of as a toxin).
2. However, few of these are large, well controlled studies.
3. These procedures can be characterized as occurring over periods that are rapid (3 days), moderate (4-30 days), or long (31+ days). Each will be considered in turn.

[References:

Amass, L., Bickel, W.K., Higgins, S.T., Hughes, J.R. A preliminary investigation of outcome following gradual or rapid buprenorphine detoxification. *J. Addict. Dis.* 13, 33-45, 1994.

Cheskin L.J., Fudala P.J., Johnson R.E. A controlled comparison of buprenorphine and clonidine for acute detoxification from opioids. *Drug Alcohol Depend* 36:115-121, 1994.

Diamant, K., Fischer, G., Schneider, C., Lenzinger, E., Pezawas, L., Schindler, S., Eder, H. 1998. Outpatient opiate detoxification treatment with buprenorphine: Preliminary investigation. *Eur. Addict. Res.* 4, 198-202.

Jasinski, D.R., Pevnick, J.S., Griffith, J.D. 1978. Human pharmacology and abuse potential of the analgesic buprenorphine. *Arch. Gen. Psychiatry* 35, 501-516.

Nigam A.K., Ray R., Tripathi B.M. Buprenorphine in opiate withdrawal: a comparison with clonidine. *J Subst Abuse Treatment* 10: 391-394, 1993.

O'Connor, P.G., Carroll, K.M., Shi, J.M., Schottenfeld, R.S., Kosten, T.R., Rounsaville, B. 1997. Three methods of opiate detoxification in a primary care setting: A randomized trial. *Ann. Inter. Med.* 127, 526-530.]

Withdrawal Using Buprenorphine

Withdrawal in 3 days

Most experience to date has been with the analgesic form of buprenorphine

Relatively low doses of buprenorphine given 2-3 times per day (i.m.), usually an inpatient setting

Well accepted by patients

Opioid withdrawal signs and symptoms suppressed (better than clonidine)

1. The analgesic form of buprenorphine is available only as an injection. It is possible to use the sublingual form of buprenorphine for opioid withdrawal, but since this sublingual form has not been available for general clinical use, physicians have been using the analgesic form for this purpose.
2. There has been concern about the legality of using the analgesic form of buprenorphine in this way (since this form of buprenorphine is not approved for the use of opioid dependence or withdrawal).
3. The next slide shows a sample dosing schedule.

Withdrawal Using Buprenorphine

Withdrawal in 3 days (continued)

Sample dosing schedule:

First day: 0.3-0.6 mg i.m. tid

Second day: 0.15-0.3 mg i.m. tid

Third (last) day: 0.15 mg i.m. bid or qd

Withdrawal Using Buprenorphine

Withdrawal in 3 days (continued)

Could also use sublingual tablets:

First day: 12 mg sl

Second day: 12 mg sl

Third (last) day: 6 mg sl

1. There have been reports of clinical experience using the analgesic form of buprenorphine for such rapid withdrawals.
2. This early experience has been limited to the analgesic form, usually by injection. Some clinicians have administered the analgesic form under the tongue, or had pharmacies create special preparations (such as buprenorphine gels) for use sublingually.
3. Based on the experience with use of injected buprenorphine for management of opioid withdrawal, it is possible to create a schedule that utilizes the sublingual tablet form of buprenorphine.

Withdrawal Using Buprenorphine

Withdrawal in 3 days (continued)

Effective in suppressing withdrawal symptoms

Long-term efficacy not known

1. Use of buprenorphine for these short periods is effective for the suppression of opioid withdrawal symptoms – especially when compared to clonidine.
2. However, the long-term outcome from such short period withdrawals is not known. In general, clinical experience indicates that short term opioid withdrawal treatment does not lead to long-term opioid abstinence (regardless of the medication used).

Withdrawal Using Buprenorphine

Withdrawal in 3 days (rapid)

Withdrawal over 4 to 30 days (moderate period)

Withdrawal over more than 30 days (long term)

1. For purposes of this discussion, moderate period withdrawal is being defined as time intervals between 4-30 days in length.

Withdrawal Using Buprenorphine

Withdrawal over 4-30 days

Few studies of buprenorphine for such time periods

Buprenorphine more effective than clonidine over this time period

However, outcomes not as good as longer periods of buprenorphine withdrawal

1. There are very few reports on use of buprenorphine for opioid withdrawal over this time period.
2. Outcomes such as treatment retention and abstinence from illicit opioids during the buprenorphine withdrawal period are not as good for these moderate period withdrawals compared to longer period withdrawals.

Withdrawal Using Buprenorphine

Withdrawal in 3 days (rapid)

Withdrawal over 4 to 30 days (moderate period)

Withdrawal over more than 30 days (long term)

1. For purposes of this discussion, long period withdrawal is being defined as time intervals greater than 30 days in length.

Withdrawal Using Buprenorphine

Withdrawal over >30 days

Not a well studied topic

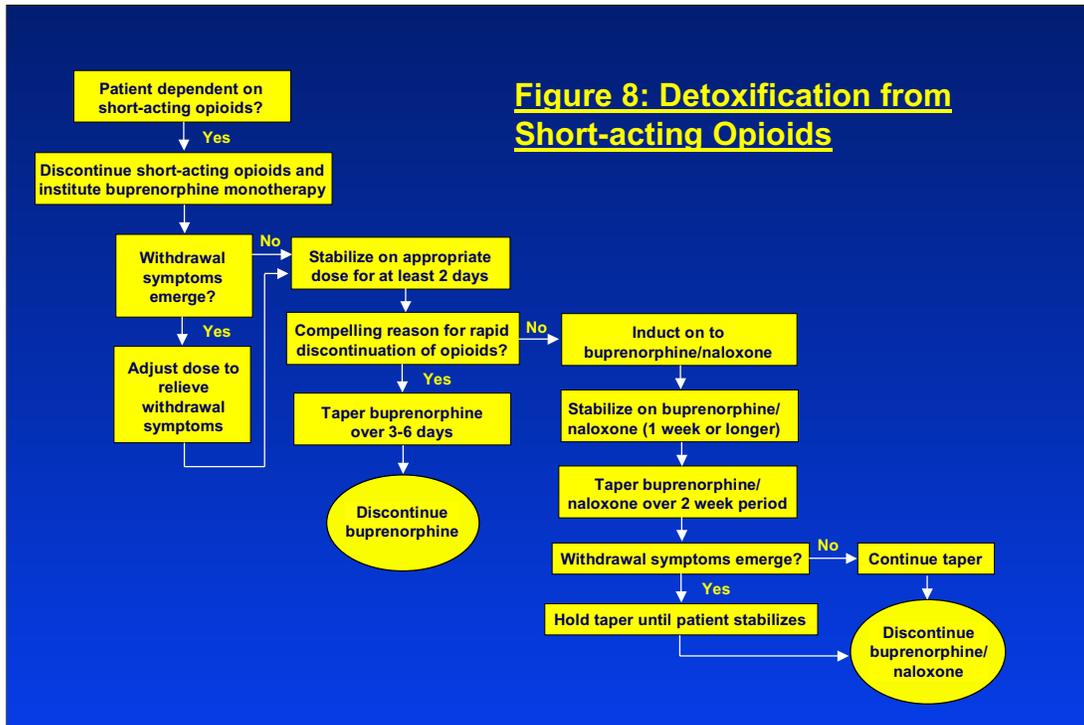
Literature on opioid withdrawal can provide guidance;
suggests longer, gradual withdrawals more effective
than shorter withdrawals

1. There are few reports on use of buprenorphine for withdrawal over this time period.
2. Literature on use of methadone for opioid withdrawal can suggest some general guidelines and recommendations.
3. For example, in a study of methadone withdrawal, patients undergoing a 10 week dose reduction (i.e., 10% per week) had a higher rate of opioid positive urine samples than those undergoing a 30 week dose reduction (i.e., 3% per week). By analogy, this suggests longer, more gradual buprenorphine withdrawals should be better tolerated and have better outcomes (as measured by urine results for illicit opioids) than more rapid withdrawals.

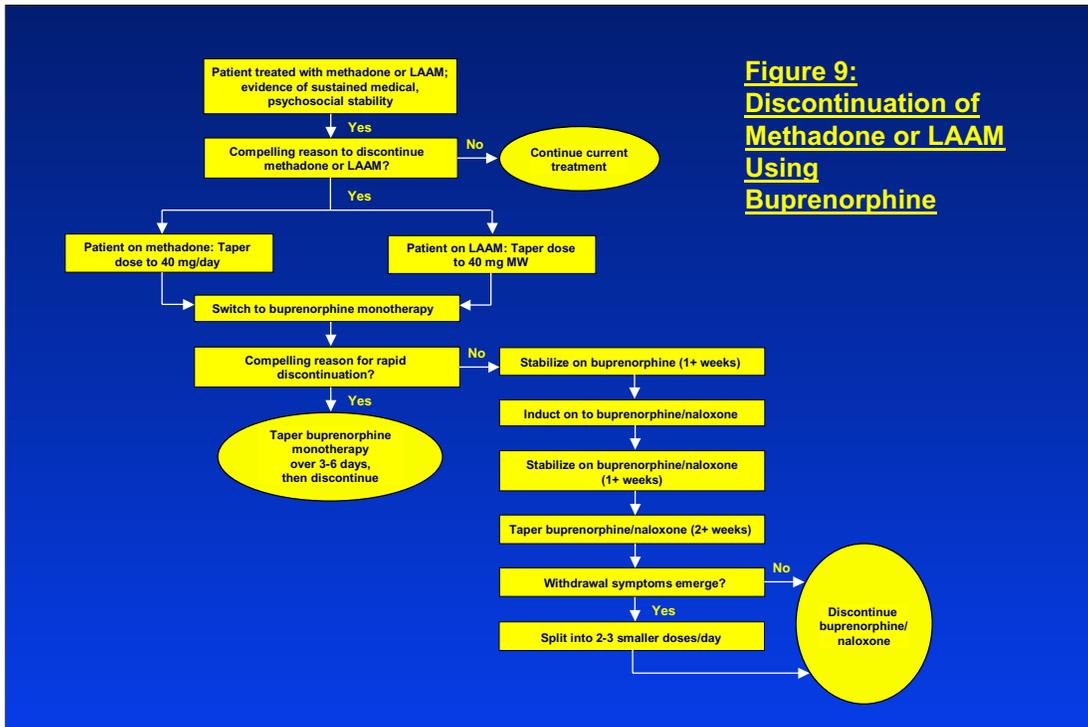
[Reference:

Senay E.C., Dorus W., Goldberg F., Thornton W. Withdrawal from methadone maintenance: Rate of withdrawal and expectations. Arch Gen Psychiatry 34:361-367, 1977.]

Figure 8: Detoxification from Short-acting Opioids



**Figure 9:
Discontinuation of
Methadone or LAAM
Using
Buprenorphine**



Outline for This Talk

- I. Efficacy of buprenorphine
- II. Safety of buprenorphine
- III. Clinical use of buprenorphine
- IV. Summary**

Summary

Buprenorphine is effective and safe when used for maintenance treatment of opioid dependence

Close monitoring of patient required during induction with buprenorphine; best to keep patient at office for several hours on first day of buprenorphine treatment

Efficacy of buprenorphine in management of withdrawal not well determined, but withdrawal from buprenorphine may be milder than withdrawal from other opioids; probably best if conducted over longer periods

Appendix to
Applied Pharmacology :
Other Medications Used
for the Treatment of Opioid Dependence

This appendix provide a brief overview to the other medications approved and/or commonly used to treat opioid dependence. This is not meant to be a comprehensive review of these pharmacotherapies. It is meant to familiarize the clinician with some of the primary features of these medications.

It is important for the clinician to have some familiarity with these medications. Patients who are treated with some of them (e.g., methadone, LAAM) may seek out office-based buprenorphine treatment. Alternately, the clinician may refer buprenorphine-maintained patients to other treatment providers who use these medications (for example, if the patient is doing poorly on buprenorphine).

Other Medications

Methadone

L-alpha-acetylmethadol (LAAM)

Naltrexone

Clonidine

1. To establish the larger context, and to show how buprenorphine fits into the overall clinical picture, we will review all the medications used in pharmacological treatment of opioid dependence.
2. We'll start with the ...most commonly used medication for the treatment of opioid dependence – methadone. There are at least 180,000 patients treated in federally licensed methadone programs in the United States.
3. Use of methadone and LAAM to treat opioid dependence is restricted to specifically licensed treatment programs which must comply with requirements established by the Food and Drug Administration (FDA) and the Drug Enforcement Agency (DEA). It is expected that this responsibility will shift to the Center for Substance Abuse Treatment (CSAT) when a new model of accreditation for these programs is instituted.

Methadone Treatment

Important to note that federal regulations require that “methadone treatment” include more than the administration of methadone medication

Methadone treatment typically includes concurrent non-pharmacological services that can enhance outcome

However, harder to standardize the delivery and quality of this non-pharmacological treatment

1. Although it is governed by federal regulations, methadone treatment can vary widely between programs – in the doses used, the length of time patients are withdrawn off methadone, and in the types of non-pharmacological treatments provided. This wide variability in methadone treatment programs is mirrored in the wide variability in outcomes found.

[References:

Strain E.C., Stitzer M.L. Methadone Treatment for Opioid Dependence. Johns Hopkins University Press, Baltimore, Maryland, 1999.

Ward J., Mattick R.P., Hall W. Methadone Maintenance Treatment and Other Opioid Replacement Therapies. Harwood Academic Publishers, Australia, 1998.]

Methadone

Pharmacology

Efficacy

Safety and side effects

Government regulation of methadone treatment

1. We'll begin with a brief review of methadone's pharmacology.

Methadone Pharmacology

- Full mu agonist opioid (mildly reinforcing)
- Good oral bioavailability
- Moderate/long duration of action
- Suppresses spontaneous opioid withdrawal
- Blocks acute effects of other opioids (e.g., heroin)

1. Methadone's profile of effects make it an excellent medication for use in the treatment of opioid dependence.

Methadone

Pharmacology

Efficacy

Safety and side effects

Government regulation of methadone treatment

Methadone Efficacy

More effective than placebo

Efficacy of the medication is related to the dose

Controlled studies have tested doses as high as 100 mg per day

Good treatment retention

Decreased illicit opioid use (urines, self reports)

Improvements in other areas found, also

1. Numerous studies have reported on the efficacy of methadone. These have included naturalistic reports, as well as double-blind, controlled clinical trials.
2. In addition to the improvements expected with methadone (i.e., on drug use), methadone treatment results in better outcomes in other areas such as other drug use, employment, and criminal activity.

[References:

Dole V.P., Nyswander M. A medical treatment for diacetylmorphine (heroin) addiction: A clinical trial with methadone hydrochloride. *JAMA* 193:80-84, 1965.

Hubbard R.L., Marsden M.E., Rachal J.V., Harwood H.J., Cavanaugh E.R., Ginzburg H.M. *Drug Abuse Treatment: A National Study of Effectiveness*. The University of North Carolina Press, Chapel Hill, North Carolina, 1989.

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Strain E.C., Stitzer M.L., Liebson I.A., Bigelow G.E. Randomized controlled trial of moderate versus high dose methadone in treatment of opioid dependence. *JAMA* 281:1000-1005, 1999.]

Methadone Efficacy

Ball and Ross study (1991)

Examined 388 patients in methadone treatment

IVDU decreased from 81% to 29% in 4 years

For 105 patients who left treatment, 82% with IVDU in 1 year

1. This study was conducted in the late 1980s, and examined outcomes in six methadone treatment programs on the east coast of the United States (Baltimore, Philadelphia, and New York).
2. For the population of 388 patients in treatment, all were previous IVDUs, although some were not actively injecting drugs at the time of admission to methadone treatment. Thus, 81% were IVDUs at the time of admission, and after 4 years of methadone treatment, this had dropped to 29%.
3. Among 105 patients who entered methadone treatment and then subsequently left, interviews in the community were conducted one year later. All were men, and 39% of them obtained some further methadone treatment in the subsequent year. Relapse to IVDU occurred frequently in the 105 men; 46% relapsed within 1-3 months of leaving treatment, and 82% had relapsed to IVDU within the year.

[Reference:

Ball J.C., Ross A. The Effectiveness of Methadone Maintenance Treatment. Springer-Verlag, New York, 1991; pages 166-168; 181-182.]

Methadone Efficacy

HIV Seroconversion

Study of two cohorts of HIV negative patients (152 patients in methadone treatment, 103 active IV opioid abusers)

18 month follow-up

HIV seroconversion:

3.5% among methadone patients

22% among active IV opioid abusers

1. This study followed patients prospectively. All were from the same neighborhood area, and follow-up assessments were conducted every 6 months (including HIV testing).

[Reference:

Metzger, D.S., Woody G.E., McLellan A.T., O'Brien C.P., Druley P., Navaline H., DePhilippis D., Stolley P., Abrutyn E. Human immunodeficiency virus seroconversion among intravenous drug users in- and out-of-treatment: an 18-month prospective study. *J Acquir Immune Defic Synd* 6:1049-56, 1993.]

Methadone

Pharmacology

Efficacy

Safety and side effects

Government regulation of methadone treatment

Methadone Safety and Side Effects

Chronic use of methadone is associated with typical side effects of mu agonist opioids (e.g., constipation, increased sweating, sexual dysfunction)

No serious adverse effects (i.e., no hepatotoxicity, no organ damage)

[References:

Kreek M.J. Medical safety and side effects of methadone in tolerant individuals. *JAMA* 223:665-668, 1973.

Kreek M.J., Dodes L., Kane S., Knobler J., Martin R. Long-term methadone maintenance therapy: Effects on liver function. *Ann Int Med* 77:598-602, 1972.]

Methadone Safety and Side Effects

No significant psychomotor/cognitive performance impairments with chronic methadone dosing

Overdose with methadone can be fatal, due to respiratory depression

Combination of methadone with other depressants can also be fatal

1. There is no evidence of psychomotor or cognitive performance problems with methadone maintenance.
2. There is a risk of fatality associated with overdose. While rare, there have been occasional reports of a non-dependent person ingesting a take home dose of methadone, and then suffering respiratory arrest. In addition, a person physically dependent on opioids (either illicit opioids or licit opioids such as methadone) can suffer respiratory arrest with a sufficiently high dose of methadone. However, access to such high doses of methadone is generally not available to patients.

[References:

Gordon N.B. Reaction-times of methadone treated ex heroin addicts. *Psychopharmacol (Berl)* 16:337-344, 1970.

Gordon N.B., Warner A., Henderson A. Psychomotor and intellectual performance under methadone maintenance. In: Committee on Problems of Drug Dependence, Minutes of the Twenty-ninth Meeting. National Academy of Sciences, Washington, D.C., 1967.

Gritz E.R., Shiffman S.M., Jarvik M.E., Haber J., Dymond A.M., Cogler R., Charuvastra V., Schlesinger J. Physiological and psychological effects of methadone in man. *Arch Gen Psychiatry* 32:237-242, 1975.]

Methadone

Pharmacology

Efficacy

Safety and side effects

Government regulation of methadone treatment

Regulation of Methadone Treatment

The governmental regulation of methadone for the treatment of opioid dependence is quite specific and detailed; it occurs at the federal and state levels, and can also occur at the local level

Dispensing methadone for treatment of opioid dependence can only occur in special clinics

Further regulations possible (and common) at state and local levels

1. The governmental regulation of methadone for the treatment of opioid dependence is quite specific and detailed. It occurs at the federal and state levels, and can also occur at the local level.
2. Current federal regulations originate from the FDA and DEA. However, responsibility for these regulations is being transferred to SAMHSA, and the regulations are being extensively revised. Final regulations are expected in early 2001.
3. For the treatment of pain, methadone can be prescribed just as any other schedule II opioid.

[References:

Federal Register July 22, 1999; Volume 64, Number 140, pages 39809-39857.

Parrino M.W. State Methadone Treatment Guidelines; Treatment Improvement Protocol (TIP) Series 1. Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Treatment, Rockville, Maryland, 1993.

Rettig R.A., Yarmolinsky A. (eds). Federal Regulation of Methadone Treatment. Institute of Medicine. National Academy Press, Washington D.C., 1995.]

Other Medications

Methadone

L-alpha-acetylmethadol (LAAM)

Naltrexone

Clonidine

1. Next we'll review LAAM. There is a smaller number of patients treated with LAAM in the United States – probably still under 10,000 as of July 2000.

LAAM

LAAM is very similar to methadone (in terms of pharmacological effects, efficacy, safety, and regulation)

Primary difference is that LAAM can be prescribed less frequently than daily (versus daily for methadone)

1. LAAM must be dispensed through special clinics, like methadone.
2. LAAM can be used effectively when administered three times per week. Consequently, patients can reduce the number of times per week they must come to the clinic to receive their medication.
3. Current regulations (as of January, 2001) do not allow take-home doses of LAAM. This should change under new CSAT regulations.

LAAM

Pharmacology

Efficacy

Safety and side effects

Government regulation of LAAM treatment

[Reference:

Finkle B.S., Jennison T.A., Chinn D.M., Ling W., Holmes E.D. Plasma and urine disposition of 1-alpha-acetylmethadol and its principal metabolites in man. *J Analytic Toxicol* 6:100-105, 1982.

Fraser H.F., Isbell H. Actions and addiction liability of alpha-acetylmethadols in man. *J Pharmacol Exp Ther* 105:458-465, 1952.

Keats A.S., Beecher H.K. Analgesic activity and toxic effects of acetylmethadol isomers in man. *J Pharmacol Exp Ther* 105:210-215, 1952.

McMahon R.E., Culp H.W., Marshall F.J. The metabolism of alpha-dl-acetylmethadol in the rat: the identification of the probable active metabolite. *J Pharmacol Exp Ther* 149:436-445, 1965.]

LAAM Pharmacology

Like methadone:

- Full mu agonist opioid (mildly reinforcing)

- Good oral bioavailability

- Suppresses spontaneous opioid withdrawal

- Blocks acute effects of other opioids (e.g., heroin)

Differs from methadone:

- Long duration of action

1. LAAM is typically prescribed for Monday, Wednesday, and Friday. There is a compensatory increase in the Friday dose relative to the Monday and Wednesday dose (by 40%), to allow for the longer dosing interval over the weekend.

LAAM

Pharmacology

Efficacy

Safety and side effects

Government regulation of LAAM treatment

References:

Eissenberg T., Bigelow G.E., Strain E.C., Walsh S.L., Brooner R.K., Stitzer M.L., Johnson R.E. Dose-related efficacy of levo-alpha acetyl methadol for treatment of opioid dependence: a randomized clinical trial. *JAMA*. 277:1945-1951, 1997.

Ling W., Charuvastra C., Kaim S.C., Klett J. Methadyl acetate and methadone as maintenance treatments for heroin addicts. *Arch Gen Psychiatry* 33:709-720, 1976.

Ling W., Klett J., Gillis R.D. A cooperative clinical study of methadyl acetate: I. Three-times-a-week regimen. *Arch Gen Psychiatry* 35:345-353, 1978.]

LAAM Efficacy

Not as many controlled studies as methadone

Studies show efficacy similar to methadone

Efficacy is related to the dose

Good treatment retention

Decreased illicit opioid use (urines, self reports)

LAAM

Pharmacology

Efficacy

Safety and side effects

Government regulation of LAAM treatment

[References:

Fudala P.J., Vocci F., Montgomery A., Trachtenberg A.I. Levomethadyl acetate (LAAM) for the treatment of opioid dependence: a multisite, open label study of LAAM safety and an evaluation of the product labeling and treatment regulations. *J Maint Addictions* 1:9-39, 1998.

Ling W., Charuvastra C., Kaim S.C., Klett J. Methadyl acetate and methadone as maintenance treatments for heroin addicts. *Arch Gen Psychiatry* 33:709-720, 1976.]

LAAM Safety and Side Effects

Highly safe when used properly

In non-dependent person, acute dose could produce prolonged effects (e.g., respiratory depression)

Daily dosing contraindicated

Most commonly reported side effects: difficulty sleeping, constipation, sweating, nervousness

LAAM

Pharmacology

Efficacy

Safety and side effects

Government regulation of LAAM treatment

Government Regulation of LAAM Treatment

LAAM is regulated like methadone – use restricted to closed system of clinics, special regulations by FDA (with SAMHSA)

It is not used as widely as methadone

Slow acceptance of its use related, in part, to need to obtain local approval (e.g., state level)

Other Medications

Methadone

L-alpha-acetylmethadol (LAAM)

Naltrexone

Clonidine

1. The third approved medication for the outpatient treatment of opioid dependence is naltrexone.

Naltrexone

Pharmacology

Efficacy

Safety and side effects

Government regulation of naltrexone treatment

Naltrexone Pharmacology

Opioid antagonist (no effects in non-dependent person,
precipitated withdrawal in opioid dependent person)

No agonist properties; no reinforcing effects to add to the
patient's motivation to continue taking naltrexone

Effectively blocks effects of opioids (e.g., heroin)

Good oral bioavailability

Long duration of action

1. Naltrexone differs from methadone and LAAM in that it is an opioid antagonist. Thus, it is not mildly reinforcing (like methadone and LAAM). This means that compliance in taking naltrexone is often poor unless the patient is highly motivated to remain free from opioid use.
2. Like methadone and LAAM, naltrexone blocks the effects of other opioids (such as heroin). However, since it is not mildly reinforcing, compliance with taking the medication is highly variable. For patients who take naltrexone, it can be very effective.
3. The goal of treatment with naltrexone, methadone, and LAAM is the same – cessation of illicit opioid use. However, naltrexone's mechanism is very different from methadone's and LAAM's.
4. Naltrexone's plasma half-life is 4 hours. The active metabolite 6-beta-naltrexol has a half-life of 12 hours. However, studies have shown that the duration of naltrexone's effects is longer than would be predicted by its half-life.
5. A risk of naltrexone treatment for opioid dependence is the potential for a serious opioid overdose after stopping naltrexone use and relapsing. For the patient who has been maintained on naltrexone, the risk of overdose death is increased due to the loss of tolerance while maintained on naltrexone. If the patient stops taking naltrexone after regular and prolonged maintenance on it, and then uses his/her usual dose of heroin, he/she may experience excessive opioid agonist effects (and even death) due to this loss of tolerance. While this potential is small, it is useful to caution naltrexone-maintained patients about this possibility.

Naltrexone

Pharmacology

Efficacy

Safety and side effects

Government regulation of naltrexone treatment

References:

Mello N.K., Mendelson J.H., Kuehnle J.C., Sellers M.S. Operant analysis of human heroin self-administration and the effects of naltrexone. *J Pharmacol Exp Ther* 216:45-54, 1981.

Walsh S.L., Sullivan J.T., Preston K.L., Garner J.E., Bigelow G.E. Effects of naltrexone on response to intravenous cocaine, hydromorphone and their combination in humans. *J Pharmacol Exp Ther* 279:524-538, 1996.]

Naltrexone Efficacy

Highly effective in controlled, inpatient studies

Can be taken daily or three times per week

Compliance and treatment retention are poor in general in outpatient clinical trials

Compliance is better in motivated patients (e.g., physicians, business professionals)

1. In outpatient studies with naltrexone, treatment retention has been found to be quite poor. For example, in a clinical trial of 242 opioid dependent patients who received at least one dose of naltrexone, 60 remained in treatment for at least two months, and only 3 took naltrexone for more than a year.
2. Naltrexone is most effective when patients have a strong motivating factor that increases the likelihood of compliance in taking the medication. For example, linking naltrexone compliance to maintenance of a medical license can be an effective strategy in a physician with a history of opioid abuse. It may also be useful in the criminal justice population.
3. Naltrexone can be taken either daily or three times per week – both schedules have equal efficacy. The latter schedule may help a patient in maintaining compliance.

[References:

Greenstein R.A., O'Brien C.P., McLellan A.T., Woody G.E., Grabowski J., Long M., Coyle-Perkins G., Mittor A. Naltrexone: a short-term treatment for opioid dependence. *Am J Drug Alcohol Abuse* 8:291-300, 1981.

Grabowski J., O'Brien C.P., Greenstein R., Ternes J., Long M., Steinberg-Donato S. Effects of contingent payment on compliance with a naltrexone regiment. *Am J Drug Alcohol Abuse* 6:355-365, 1979.

Tilly J., O'Brien C.P., McLellan A.T., Woody G.E., Metzger D.S., Cornish J. Naltrexone in the treatment of federal probationers. In: *Problems of Drug Dependence 1991, Proceeding of the 53rd Annual Scientific Meeting, The Committee on Problems of Drug Dependence, Inc.*, Harris L. (ed). NIDA Research Monograph 119, Rockville, Maryland, p 458, 1992.

Washton A.M., Gold M.S., Pottash A.C. Successful use of naltrexone in addicted physicians and business executives. *Adv Alcohol Subst Abuse* 4:89-96, 1984.]

Naltrexone

Pharmacology

Efficacy

Safety and side effects

Government regulation of naltrexone treatment

Naltrexone Safety and Side Effects

Very safe in usual dose range

Higher than usual doses may produce increases in liver function tests (LFTs)

Most commonly reported side effects are abdominal complaints and dysphoria (although both are rare)

1. The usual daily dose of naltrexone for the treatment of opioid dependence is 50 mg. It can also be dosed on a Monday/Wednesday/Friday schedule (100/100/150 mg).
2. Reports of increased liver function tests (LFTs) were in studies of obese patients, and studies of patients with dementia, who were being treated with high doses of naltrexone (e.g., 300+mg per day).
3. Can use naltrexone in patients with high LFTs at baseline (up to 3x normal) – just need to monitor LFTs.
4. If rise in LFTs occurs, typically resolves with discontinuation of naltrexone.

[Reference:

Pfohl D.N., Allen J.I., Atkinson R.L., Knopman D.S., Malcolm R.J., Mitchell J.E., Morley J.E. Naltrexone hydrochloride (Trexan): A review of serum transaminase elevations at high dosage. In: Problems of Drug Dependence 1985, Proceedings of the 47th Annual Scientific Meeting, The Committee on Problems of Drug Dependence, Inc., Harris L. (ed). National Institute on Drug Abuse Research Monograph 67, Rockville, Maryland, pp. 66-72, 1986.]

Naltrexone

Pharmacology

Efficacy

Safety and side effects

Government regulation of naltrexone treatment

Government Regulation of Naltrexone Treatment

Not scheduled; no abuse potential

No special regulations governing naltrexone use

1. Naltrexone is not scheduled, and there is no abuse of naltrexone.

Other Medications

Methadone (opioid agonist)

L-alpha-acetylmethadol (LAAM) (opioid agonist)

Naltrexone (opioid antagonist)

Clonidine (alpha 2 adrenergic agonist)

1. Methadone and LAAM are opioid agonists, and naltrexone is an opioid antagonist. In contrast, clonidine does not interact directly with the opioid system – it is an alpha 2 adrenergic agonist (as will be reviewed in subsequent slides).
2. Clonidine is not approved for the treatment of opioid dependence, but it is commonly used “off label” for purposes of withdrawing patients off opioids. Since clonidine is not an opioid, it can be used off label in this way. Because of this common use, it is reviewed here.

Clonidine

Pharmacology

Efficacy

Safety and side effects

Government regulation of clonidine

Clonidine Pharmacology

Alpha 2 adrenergic agonist

Effective antihypertensive (primary indication)

Good oral bioavailability

Relatively short half-life

1. The half-life of clonidine is 12-16 hours.
2. Usual dosing with clonidine for the treatment of opioid withdrawal is three times per day.

Clonidine

Pharmacology

Efficacy

Safety and side effects

Government regulation of clonidine

References:

Camí J., de Torres S., San L., Solé A., Guerra D., Ugena B. Efficacy of clonidine and of methadone in the rapid detoxification of patients dependent on heroin. *Clin Pharmacol Ther* 38:336-341, 1985.

Charney D.S., Sternberg D.E., Kleber H.D., Heninger G.R., Redmond D.E. The clinical use of clonidine in abrupt withdrawal from methadone. *Arch Gen Psychiatry* 38:1273-1277, 1981.

Cheskin L.J., Fudala P.J., Johnson R.E. A controlled comparison of buprenorphine and clonidine for acute detoxification from opioids. *Drug Alcohol Depend* 36:115-121, 1994.

Gold M.S., Redmond D.E., Kleber H.D. Clonidine blocks acute opiate-withdrawal symptoms. *Lancet* 599-602, September 16, 1978.

Gossop M. Clonidine and the treatment of the opiate withdrawal syndrome. *Drug Alcohol Depend* 21:253-259, 1988.

Rounsaville B.J., Kosten T., Kleber H. Success and failure at outpatient opioid detoxification: evaluating the process of clonidine- and methadone-assisted withdrawal. *J Nerv Ment Dis* 173:103-110, 1985.]

Clonidine Efficacy

Effective in diminishing opioid withdrawal signs after abrupt discontinuation of opioids

Less effective at decreasing subjective withdrawal symptoms

Can be used orally or in a patch (both forms effective)

1. Studies have shown that clonidine is effective at decreasing opioid withdrawal signs. However, it is less effective at attenuating the subjective effects of withdrawal – so that patient looks good, but does not feel good.

Clonidine

Pharmacology

Efficacy

Safety and side effects

Government regulation of clonidine

[References:

Charney D.S., Sternberg D.E., Kleber H.D., Heninger G.R., Redmond D.E. The clinical use of clonidine in abrupt withdrawal from methadone. *Arch Gen Psychiatry* 38:1273-1277, 1981.

Cheskin L.J., Fudala P.J., Johnson R.E. A controlled comparison of buprenorphine and clonidine for acute detoxification from opioids. *Drug Alcohol Depend* 36:115-121, 1994.

Gossop M. Clonidine and the treatment of the opiate withdrawal syndrome. *Drug Alcohol Depend* 21:253-259, 1988.]

Clonidine Safety and Side Effects

Primary risk of patients becoming hypotensive

Some reports that clonidine is sedating

Some reports of clonidine abuse

1. The primary risk associated with clonidine use is that the patient will become hypotensive.
2. In addition, studies testing the efficacy of clonidine in the treatment of opioid withdrawal have found patients report sedating effects.
3. Urine testing for drugs of abuse do not routinely test for clonidine. However, there have been reports of patients who abuse clonidine.

[References:

Anderson F., Paluzzi P., Lee J., Huggins G., Svikis D. Illicit use of clonidine in opiate-abusing pregnant women. *Obstet Gynecol* 90:790-4, 1997.

Conway T., Balson A. Concomitant abuse of clonidine and heroin. *Southern Med J* 86:954-6, 1993.]

Clonidine

Pharmacology

Efficacy

Safety and side effects

Government regulation of clonidine

Government Regulation of Clonidine

Not scheduled

Not approved for use in treatment of opioid withdrawal (i.e., off-label use)

No special regulations for use in treatment of opioid withdrawal

1. While clonidine is not scheduled, the reports of abuse of clonidine suggest some caution in its use among patients with substance abuse.

Other Medications

Finally, while the emphasis of this section has been medications, it is important to note that optimal outcomes with medications occur when combined with non-pharmacological treatments (counseling, group therapy, behavioral interventions)

Pharmacotherapy alone is rarely sufficient

1. Finally, while this talk is focusing on medications, a brief comment should be made about the role of concurrent non-pharmacological treatments for opioid dependence.

[Reference:

McLellan A.T., Arndt I.O., Metzger D.S., Woody G.E., O'Brien C.P. The effects of psychosocial services in substance abuse treatment. *JAMA* 269:1953-9, 1993.]

Summary

Several medications are available for the treatment of opioid dependence and withdrawal

When used properly, these medications can be safe and highly effective

The clinician using office-based buprenorphine should be aware of these medications, as patients maintained on them may seek to transfer to buprenorphine, and for some patients, a transfer to these other medications may be indicated

1.

Non-Pharmacological Treatment

Role of Non-Pharmacological Treatments

There are two overall goals of treatment for opioid dependence. The first is **sustained abstinence** from substance use. Abstinence does not mean the patient is no longer maintained on a therapeutic medication. Rather, it means the patient has achieved complete cessation of non-medically supervised substance use. The second goal is the achievement of **treatment stability**. This goal includes abstinence, but also represents stabilization in other aspects of the patient's life.

1. In order to understand the role of non-pharmacological interventions in the treatment of opioid dependence, we will begin by making some general points about the goals of substance abuse treatment for opioids.
2. Specifically, we will talk about what is meant by the term “abstinence” and the concept of “treatment stability.”
3. The goals of treatment include the specific goal of sustained abstinence, but also the broader goal of treatment stability. Abstinence as used here means the complete cessation of non-medically supervised psychoactive substance use. The term abstinence is not meant to imply that the patient does not take any psychoactive substances; thus, the buprenorphine maintained patient may achieve abstinence (from other opioid use, or from all non-medically supervised psychoactive substance use), while maintained on a psychoactive substance (buprenorphine). However, this maintenance is under the supervision of a physician.
4. The term treatment stability is then meant to include abstinence, but represents more than just abstinence. It is the achievement of stability in the other aspects of life that have often been adversely effected by substance use – for example, the emotional, physical, and spiritual realms of life. “Treatment stability” does not mean that there are no problems in these areas. Rather, it means that the problems in these areas are typical and are not uniquely attributable to the use of substances.

Treatment with medications such as buprenorphine provide an important mechanism for achieving and maintaining **abstinence**. However, non-pharmacological interventions are nearly always necessary to achieve **treatment stability**.

1. Understanding the distinction between abstinence and treatment stability then allows us to understand the role of medications such as buprenorphine. Buprenorphine can be highly effective in the achievement and maintenance of abstinence from non-medically supervised opioid use. However, it does not address these other problem areas that require resolution in the process of achieving treatment stability. It is non-pharmacological interventions that are nearly always required to achieve treatment stability.
2. Thus, the importance of the present talk on non-pharmacological treatments.

This section reviews non-pharmacological aspects of substance abuse treatment. The purpose of the section is two-fold. First, to provide a review of the different levels of treatment intensity used with substance abuse patients, and second, to briefly review the types of treatments that may be used in different levels of services.

1. There are three purposes to this talk.

These non-pharmacological treatments are an important aspect of buprenorphine treatment. They can enhance response to buprenorphine (aiding in the achievement and maintenance of **abstinence**), and they can facilitate the goal of **treatment stability**.

1. Non-pharmacological treatments have important roles in both the achievement of abstinence, as well as facilitating the goal of treatment stability.
2. Many treatment elements, each serving a different purpose, may be required.

Outline for This Talk

- I. Levels of treatment intensity
- II. Types of interventions used concurrently with pharmacological treatments
- III. Summary

1. Each of these topics will be addressed in turn during the course of this lecture.
2. This lecture cannot provide a full review of all aspects of many of the topics reviewed. The purpose here is to provide a few highlights that can help the practitioner understand the range of treatment options which may be indicated for a particular patient.

Outline for This Talk

- I. Levels of treatment intensity
- II. Types of interventions used concurrently with pharmacological treatments
- III. Summary

1. The American Society of Addiction Medicine (ASAM) has developed criteria for matching patients with the appropriate intensity of treatment services. The Patient Placement Criteria (PPC) describe the following treatment settings and the types of treatments and the levels of treatment intensity associated with them:

- Early intervention
- Outpatient services
- Intensive outpatient/partial hospitalization
- Residential/inpatient services
- Medically-managed intensive inpatient services

2. Here, we'll review these treatment settings, although we won't use these exact categories.

[Reference:

American Society of Addiction Medicine. Patient Placement Criteria for the Treatment of Substance-Related Disorders, Second Edition (ASAM PPC-2). American Society of Addiction Medicine, Chevy Chase, Maryland, 1996.]

Levels of Treatment Intensity

Outpatient (OP)

Intensive Outpatient (IOP)

Day or Partial Hospitalization Program (PHP)

Residential Rehabilitation/Inpatient

Recovery Residence

Office Setting

1. We'll begin by talking about outpatient treatment (OP).

Outpatient (OP)

Low intensity and long term treatment

Generally 2-4 hours per week for several months

Targeted at individuals with minimal co-occurring problems, good insight, compliant, supportive environment, low symptomatology

Useful when combined with pharmacotherapy – e.g., smoking cessation

1. Outpatient treatment can include individual counseling and therapy, as well as group treatments.
2. Patients may transition from more intensive levels of services to Outpatient treatment, and initially require 2-4 hours per week of treatment (e.g., two groups each week and one individual session). As time in Outpatient treatment progresses, the intensity per week may decrease (e.g., to one per week visits, or even less).
3. A model of Outpatient substance abuse treatment in office based practice is treatment provided by some physicians for smoking cessation. That treatment can include medication (nicotine substitution, bupropion) and on-site non-pharmacological services such as individual counseling provided by the physician or a nurse, and/or a group of patients (all working on stopping smoking) lead by a health care professional (e.g., a nurse).

Levels of Treatment Intensity

Outpatient (OP)

Intensive Outpatient (IOP)

Day or Partial Hospitalization Program (PHP)

Residential Rehabilitation/Inpatient

Recovery Residence

Office Setting

1. Moving up a continuum in terms of intensity of treatment and monitoring of the patient, the next level of service is intensive outpatient treatment.
2. While the ASAM PPC includes this with Partial Hospitalization Programs (PHPs), we will consider Intensive Outpatient Programs separate from Partial Hospitalization Programs.

Intensive Outpatient (IOP)

Day or evening program

Typically 9+ hours per week

For patients who don't need to be completely removed from their living environment/work, but need intermediate level of support with frequent therapeutic contact

1. Intensive Outpatient Programs (IOPs) are often related to Partial Hospitalization Programs (PHPs), so that patients may transition from a Partial Hospitalization Program to an Intensive Outpatient Program as they progress in their treatment.
2. A typical Intensive Outpatient Program may have a patient attend the program 3 days per week (MWF), for 3 hours of treatment each day.

Levels of Treatment Intensity

Outpatient (OP)

Intensive Outpatient (IOP)

Day or Partial Hospitalization Program (PHP)

Residential Rehabilitation/Inpatient

Recovery Residence

Office Setting

1. Services provided in a Partial Hospitalization Program are more intensive than those provided in an Intensive Outpatient Program, and Partial Hospitalization Program is the most intensive level of service provided on an outpatient basis.

Day or Partial Hospitalization Program (PHP)

Similar to residential or inpatient in terms of substance abuse treatment intensity

Patient needs daily structure, but can remain abstinent for brief periods of time without staff supervision

Patients live at home or in associated housing

1. Partial Hospitalization Programs typically provide 6 (or more) hours per day of actual treatment. Allowing for other time commitments during the day – for example, for meals – the total time at a program may be 8 or more hours each day. Programs may operate as often as seven days per week.

2. Services provided can include group and individual therapies, as well as other services (occupational therapy, vocational and educational training, art therapy, etc.). Medical treatments provided in a Partial Hospitalization Program can be intensive as well – including, in some cases, intravenous lines and wound care.

Levels of Treatment Intensity

Outpatient (OP)

Intensive Outpatient (IOP)

Day or Partial Hospitalization Program (PHP)

Residential Rehabilitation/Inpatient

Recovery Residence

Office Setting

1. These first three settings for treatment are interrelated, and often can be delivered by the same staff at the same setting (varying the amount of time the patient spends at the program).
2. We'll next review the primary distinguishing features of residential rehabilitation and inpatient programs. These programs involve a significant shift in type of treatment provided (not just the amount), since the patient is staying and being monitored by staff for 24 hours. This is the most intensive level of therapy utilized for substance abuse treatment.

Residential Rehabilitation/Inpatient

Constant monitoring by on-site staff

Ability to manage patients who are medically complicated (inpatient) or not medically complicated (residential)

Patients often have failed less intensive levels of treatment

Staff with substance abuse treatment experience

1. The primary distinguishing feature of these programs is that 24 hour, on-site supervision is provided.
2. This supervision may be medically intensive (inpatient) or not medically intensive (residential).
3. Patients admitted to these programs have often failed a lower level of treatment service (for example, they've failed an outpatient detoxification program). Alternately, they may have a medical co-morbidity that leads to inpatient treatment (for example, a seizure disorder in a person who is alcohol dependent and needing detoxification).

Levels of Treatment Intensity

Outpatient (OP)

Intensive Outpatient (IOP)

Day or Partial Hospitalization Program (PHP)

Residential Rehabilitation/Inpatient

Recovery Residence

Office Setting

1. The first four levels of treatment are presented in an escalating order of intensity. However, these last two levels are not more intense than the first four – rather, they are different modalities of substance abuse treatment.
2. We will begin with a brief review of recovery residences, a level of treatment that is less intensive than the ones covered so far.

Recovery Residence

Community-based living arrangement in monitored environment

Can be linked with more intensive level of service (e.g., Partial Hospitalization Programs, or Intensive Outpatient Programs)

Often has a 12 step focus

1. For example, these may be half-way houses. While on-site treatments are not prominent in these houses, it is not uncommon for 12 step meetings to occur on the premises. Members may also travel together to meetings in the local community.
2. The ASAM PPC (second edition) describes these facilities as: "...low intensity professional treatment services at least 5 hours per week (or as specified by state licensure requirements). Treatment is directed toward applying recovery skills, preventing relapse, promoting personal responsibility, and reintegrating the resident into work, education, and family life. The services may include individual, group, and family therapy. Mutual self-help meetings usually are available on-site."
3. These houses can provide a valuable resource for building a support network for patients new in the recovery process.
4. Care must be taken in selecting a recovery residence, as there can be considerable variability in their operations. In particular, some may have minimal monitoring and/or support or guidance, and residents who relapse may remain on site and lead others to relapse, too.

Levels of Treatment Intensity

Outpatient (OP)

Intensive Outpatient (IOP)

Day or Partial Hospitalization Program (PHP)

Residential Rehabilitation/Inpatient

Recovery Residence

Office Setting

1. Finally, treatment can be provided in the office setting.

Office Setting

Office setting well-suited for management of medication

To deliver other elements of substance abuse treatment (which are necessary), additional systems/services required

1. The office setting is well-suited for the deliver and monitoring of medication (buprenorphine). This setting can also be effectively used for delivering necessary elements of non-pharmacological treatments, but services and systems need to be put in place to do so. In most cases, these on-site services share features of outpatient treatment (which was reviewed earlier in this section).

Office Setting

Pharmacological management by health professional with on-going supervision of recovery related activities

Psychotherapy can be part of management (if clinician qualified)

Patient may attend 12 step meetings as part of interventions

Can include on-site group therapy

1. In addition to attending 12 step meetings, patients may reside at a recovery residence while receiving treatment through the office. They may also move in and out of more intensive levels of care (e.g., Partial Hospitalization Program, Intensive Outpatient Program) as they progress in their treatment.

Outline for This Talk

- I. Levels of treatment intensity
- II. Types of interventions used concurrently with pharmacological treatments
- III. Summary

1. That completes our review of the levels of treatment intensity that might be utilized in treating patients with substance abuse. Now we're going to review the types of treatment interventions patients may receive (in addition to medications, which we won't discuss in this lecture).

Treatment Interventions

12 Step Oriented Treatment	Self-help Groups
Group Therapy	Supportive Psychotherapy
Cognitive Behavioral	Contingency Management
Cue Exposure	Psychodynamic
Network Therapy	Community-Based Model
Couple or Family	Vocational Training
Motivational Enhancement	Relapse Prevention

1. This is not a complete list of all the different types of non-pharmacological treatments that you might hear about.
2. This section will provide very brief reviews for each of these treatment approaches. Most could be lectures unto themselves, and it's beyond the scope of this talk to provide anything more than a quick summary of their primary features. The goal is not to give you the background needed to use these modalities. Rather, it is to give you some sense of familiarity with them, so you can identify one or more as appropriate for a particular patient.
3. We'll begin with 12 step oriented treatment.

12 Step Oriented Treatment

Model emphasizes:

Complete abstinence

Psychosocial recovery

Spiritual recovery

Involvement in 12 step self-help groups

Ubiquitous, free, and offers support to all who request it

1. Twelve step programs are Alcoholics Anonymous, Narcotics Anonymous, etc.
2. Some 12 step programs, but not all, may actively discourage participants from maintenance on medications, including methadone and buprenorphine, because they believe the patient is not abstinent if they are receiving such medications. The patient maintained on a medication may need to visit different meetings to find the best fit for them.
3. These programs are widely available and helpful to many patients.
4. There is no cost to the patient for attending meetings.
5. There is a strong emphasis on maintaining anonymity.
6. There is considerable latitude in the spiritual element.
7. Patients may resist attending these programs, complaining that all attending are “hypocrites” because others who attend use drugs after a meeting. It is useful to point out to patients that the purpose of their attending these meetings is to aid in their recovery, not to monitor the progress of others. (And to encourage them to seek out other meetings if they don’t find initial ones satisfying for them.)
8. The NIAAA Twelve Step Facilitation Therapy manual is a manualized approach for helping patients engage in 12 step programs.

[References:

Alcoholics Anonymous, Third Edition. Alcoholics Anonymous World Services, Inc., New York, 1976.

Narcotics Anonymous, Fifth Edition. World Service Office, Inc., Van Nuys, California, 1983.

Nowinski J., Baker S., Carroll K. Twelve Step Facilitation Therapy Manual. National Institute on Alcohol Abuse and Alcoholism, Project MATCH Monograph Series, Matteson M.E. (ed), Volume 1. U.S. Department of Health and Human Services, NIAAA, Rockville, MD 1994.]

Self-Help Groups

Meaningful support system and the philosophical or spiritual approach to help one cope with one's condition

Influenced by both empirical orientation and mix of individuals who attend any given meeting

Ubiquitous, free, and offer support to all who request it

1. Self-help groups include 12 step programs, but include other groups as well.
2. These may be groups that meet in the physician's office or at other sites.
3. Self-help groups are not run by professionals. Rather, they are run by the participants who attend the meeting. There may be older, more experienced participants who help newer members become oriented to the operation of the group.
4. Alcoholics Anonymous and Narcotics Anonymous (and often other self-help groups) are listed in local phone books. Local offices can provide a list of the times and places of open meetings.

Group Therapy

Led by a professional

Distinguishing feature is a group of people with a similar characteristic

Wide variety of techniques can be used

Approach used can depend upon the therapist, the setting, and the patient population

1. Group therapy overlaps with 12 step groups and self-help groups (i.e., all are based upon a group of people with a similar problem gathering together to find help and support in overcoming or managing that problem).
2. However, the term “group therapy” is often used to distinguish treatment that is lead by a professional (such as a physician, nurse, or therapist). Unlike 12 step and self help groups, group therapy is usually not free.
3. The professional who leads the group may have a philosophical approach (e.g., psychoanalytic, cognitive-behavioral) that underlies the treatment provided.

Supportive Psychotherapy

Does not endorse any particular model to help with avoidance of drug use – supports individuals with their effort to achieve drug free state

Therapist is empathic, nonjudgmental, supportive

Highly adaptable to the office setting

1. Supportive psychotherapy may be provided in either an individual or group setting.
2. Supportive psychotherapy tends to focus on the “here and now” – what’s happening in the present time (rather than an emphasis on how experiences in the past are influencing current feelings, thoughts, and behaviors).
3. It can be directional (i.e., the therapist is giving the patient specific advice and recommendations).

Cognitive Behavioral

Directive psychotherapeutic technique

Therapist helps patient identify and modify thought processes and decisions that are linked to problematic behavior

1. Cognitive behavioral therapy can also be directive (like supportive psychotherapy).
2. This form of psychotherapy has been extensively studied in the treatment of depression, and shown to be quite effective in patients with mild and moderate depression.
3. In cognitive behavioral therapy, the therapist works with the patient to identify links between their thoughts and behaviors, and then to modify those patterns.

[References:

Carroll K.M. A Cognitive-Behavioral Approach: Treating Cocaine Addiction. Therapy Manuals for Drug Addiction, Manual 1. U.S. Department of Health and Human Services, National Institute on Drug Abuse, Rockville, Maryland, 1998.

Kadden R., Carroll K., Donovan D., Cooney N., Monti P., Abrams D., Litt M., Hester R. (eds) Cognitive-Behavioral Coping Skills Therapy Manual: A Clinical Research Guide for Therapists Treating Individuals With Alcohol Abuse and Dependence. National Institute on Alcohol Abuse and Alcoholism, Project MATCH Monograph Series, Volume 3. U.S. Department of Health and Human Services, National Institute on Alcohol Abuse and Alcoholism, Rockville, Maryland, 1994.]

Contingency Management

Contracting and setting up pre-determined positive or negative consequences to an event (e.g., drug use)

Studied extensively in patients abusing cocaine, illicit opioids

1. Contingency management is an approach grounded in behavior theories.
2. It is useful to note that, in general, positive reinforcement works better than negative reinforcement or punishment.
3. There have been many studies using contingency management, for example, in methadone clinics (and using take home doses of methadone – a positive reinforcer – to alter a target behavior, such as cocaine use as indicated by cocaine positive urine samples). These studies show that contingency management can be quite effective.
4. Contingency management procedures may be used in office-based treatment, by identifying rewards that are attractive to the patient. When setting up a contingency management system, the parameters (expected change in behavior, the reward, etc.) need to be clearly spelled out for everyone involved (patient, doctor, office staff, family members).

[References:

Budney A.J., Higgins S.T. A Community Reinforcement Plus Vouchers Approach: Treating Cocaine Addiction. Therapy Manuals for Drug Addiction, Manual 2. U.S. Department of Health and Human Services, National Institute on Drug Abuse, Rockville, Maryland, 1998.

Robles E., Silverman K., Stitzer M.L. Contingency Management Therapies. In: Methadone Treatment for Opioid Dependence, Strain E.C., Stitzer M.L. (eds). Johns Hopkins University Press, Baltimore, Maryland, 1999.]

Cue Exposure

Based on classic conditioning

Couples drug use stimuli with aversive stimuli

Long term results questionable

1. Cue exposure has been studied in the treatment of alcohol dependence and in smoking cessation. It is uncommonly used today.

Psychodynamic Psychotherapy

Theory used to explain mental experiences and problematic life experiences (but not limited to explaining the distress of patients)

Central features of the therapeutic process are transference and resistance

Emphasizes unconscious processes

1. Psychodynamic psychotherapy is grounded in theory that explains mental experiences and problems in the patient's life. The theory gained widespread appeal and interest for many years, although its promised power has never been realized. While still extensively practiced and taught, its influence has decreased in recent years.
2. Studies of psychodynamic psychotherapy for the treatment of substance abuse disorders have generally shown that patients may show gains in insight to their lives, but these insights are not coupled with decreases in their substance abuse.
3. Transference is displacement on to the therapist – the thoughts, feelings, and behaviors associated with some figure from the patient's life.
4. Resistance is the unconscious blocking or thwarting of therapy.

Network Therapy

Designed to be used in office practice

Patients form supportive, therapeutic networks – become involved with individuals who can help them achieve goals

1. Network therapy can be viewed as a variation on supportive psychotherapy. The therapist aids the patient in the development of supportive, therapeutic networks in their life.

Community-Based Model

Used initially with chronic, mentally ill patients

If you cannot change the individual, change the environment

1. This model has primarily been used in patients with major mental illnesses.
2. However, it has a certain relevance to substance abuse, in that one maxim heard in substance abuse treatment programs is that substance abuse patients need to “change people, places, and things.” That is, altering the environment of the patient can aid in achieving and maintaining abstinence. (However, it should be noted that another common saying in substance abuse treatment programs, and among substance abuse patients, is “once an addict, always an addict.” One interpretation of this saying is that changing people, places, and things is insufficient to address a person’s substance abuse – they must change, and they always run the risk of relapse.)
3. Note that this approach to treatment can be addressed through the use of recovery residencies, one of the treatment levels discussed in the first part of this talk. Recovery residencies seek to change the environment of the patient, in order to facilitate treatment stability.

Couple or Family Counseling

Recognizes the system in which drug using occurs

Sets out to change those system dynamics

1. Substance abuse can have a significant impact on spouses and families. However, it is probably best to seek abstinence from all problematic substance use before attempting to address and change couple and family dynamics that have been impacted by the substance abuse.
2. At the same time, involving significant others in the treatment process can be useful – for example, to help catalyze change, to help monitor medication adherence, and to help in monitoring treatment progress.

Vocational Training

Not really a treatment for substance use disorders

Recognizes that engagement in prosocial activities is supportive of recovery

1. Vocational training, like many other nonpharmacologic treatment interventions, may be best reserved for use after the patient has achieved abstinence from problematic substance use.
2. Often state-supported vocational rehabilitation programs are available for patients.
3. The role of structure – such as work or education – is extremely important in the process of recovery for a patient. Unstructured time provides opportunity for relapse. In addition to work and/or education, patients can also structure time through attendance at 12 step and other self help meetings, and through other pro-social activities such as volunteer work.

Motivational Enhancement

Therapist seeks to create situation that enhances patient's interest and desire for changing

Can be relatively brief and focused

Therapist is not an authority, but a companion and consultant to the patient

However, therapist is giving direction (but is to be gentle and subtle)

1. Motivational enhancement therapy seeks to facilitate the patient's readiness, willingness, and desire to make a change (e.g., stop substance use).
2. The therapist is not actively directive (i.e., the therapist doesn't tell the patient what they should do). However, the therapist does provide guidance to the treatment process.
3. There are five principles used by the therapist in this approach: the expression of empathy, the encouragement of developing discrepancy in the patient, the avoidance of argumentation, the rolling with resistance, and the support of self-efficacy.

[Reference:

Miller W.R., Zweben A., DiClemente C.C., Rychtark R.G. (eds) Motivational Enhancement Therapy Manual: A Clinical Research Guide for Therapists Treating Individuals With Alcohol Abuse and Dependence. National Institute on Alcohol Abuse and Alcoholism, Project MATCH Monograph Series, Volume 2. U.S. Department of Health and Human Services, National Institute on Alcohol Abuse and Alcoholism, Rockville, Maryland, 1994.]

Relapse Prevention

Method seeks to identify precipitants that can lead to relapse

Develop strategies to address these potential precipitants

Generally time limited and relatively brief

1. Relapse prevention is a treatment approach that is designed for use in patients who have stopped their substance use. While cessation of use has occurred, risk of relapse is high (especially during the early period after cessation), and relapse prevention is a method that seeks to maintain this abstinence and minimize the risk of relapse.
2. The method emphasizes the identification of precipitants to relapse (or triggers), and the development of strategies to address these situations when the patient is most vulnerable to relapse.

Treatment Interventions

12 Step Oriented Treatment	Self-help Groups
Group Therapy	Supportive Psychotherapy
Cognitive Behavioral	Contingency Management
Cue Exposure	Psychodynamic
Network Therapy	Community Based Model
Couple or Family	Vocational Training
Motivational Enhancement	Relapse Prevention

1. This completes our review of these different types of treatment interventions.

Outline for This Talk

- I. Levels of treatment
- II. Types of interventions used concurrently with pharmacological treatments
- III. Summary

Summary

Know the resources in the community – the levels of service and the modalities provided in different programs

Have a low threshold for linking patients to these treatments – pharmacological treatment alone is rarely sufficient to achieve treatment goals

While linking patients to treatment, recognize the importance, value, and potential power of non-pharmacological services provided on-site in the office setting

Appendix to
Role of Non-Pharmacological Treatments:
Principles Guiding the Non-Pharmacological
Treatment of Patients with
Substance Abuse Disorders

1. This appendix to the Role of Non-pharmacological Treatments section reviews some general principles that it is hoped will be useful in the comprehensive approach to management of patients with substance abuse disorders – especially in the setting of office-based practice. There are 16 principles reviewed here.

Principle #1

Substance abuse disorders are independent problems

Not an expression of other problems

Can co-exist with other psychological and social problems

1. First, while substance abuse disorders can co-exist with other psychological and social problems, they are not due to these other problems. Thus, for example, treating a depressive disorder will rarely result in cessation of cocaine use, but treatment of cocaine use will often result in alleviation of depressive symptoms.

Principle #2

A coordinated program is key

Treatment cannot be simply writing a prescription and/or the doctor-patient relationship alone

Many elements are necessary and serve different purposes

The patient must carry out the program with assistance from others where and when available

1. Treatment needs to be organized, coordinated, specific, and clear to all involved. That is, the patient and family, the provider, and all others who have a part in the patient's care should understand the goals of treatment, the interventions planned, and the consequences for success and failure.
2. All available resources should be used to help the patient.

Principle #3

Management of substance use disorders requires work over the long term

For most patients, there is a lifelong need to address issues of substance abuse

1. Patients and families should understand that some level of vigilance will always be required. It can be helpful to point out to the patient that their substance abuse has probably been a long time in development, and it will thus probably be at least as long to establish a solid recovery (treatment stability).
2. The idea of quick fixes will need to be addressed for some patients. Fads periodically come along which promise to fix a person's drug abuse problem quickly (phen/fen, ultrarapid detox's). These fads inevitably fail to live up their initial promise.

Principle #4

The key to success is change

Change must occur in many domains, including:

Social supports (including family, friends)

Attitudes

Environment

Activities

Patterns of thinking

Coping with feelings

Principle #5

A formal psychiatric assessment is useful

Particular attention should be directed to mood (anxiety, depression) and antisocial personality disorder

1. A formal psychiatric assessment by a professional trained to diagnose and treat psychiatric disorders can be highly useful in the management of patients – especially if difficulties have arisen that fail to fit neatly into the more common categories of psychiatric conditions. A well conducted formal psychiatric assessment considers all aspects of the patient in arriving at a formulation.
2. Not all patients must have a formal psychiatric assessment, but it can be useful to obtain such in patients who are suspected of having psychiatric difficulties.
3. A separate lecture directly addresses psychiatric co-morbidity.

Principle #6

Treatment should involve the family, when available

While ideal, this may be difficult to do

“Family” can include significant others

This should be someone who is not using/abusing drugs
or alcohol

1. Efforts should be made to include some non-substance abusing friend, family member, or associate in the patient's treatment process. Having the supportive help of such a person increases the likelihood of treatment success.
2. The physician should not be this significant other for the patient they are treating.

Principle #7

Confrontation is sometimes a necessary part of treatment

Confrontation does not mean badgering or berating

Put together evidence for your concern and make a succinct summary; be nonjudgmental; use precise diagnostic terms and tell the patient just what must be done; assess the patient's reaction and be prepared to respond to denial, anger, blaming; ask the patient if the family would agree with your findings

1. Don't avoid confrontation, but don't seek it out either.
2. Examples of situations that might require confrontation are the discovery that the patient has been selling their buprenorphine prescription, that they have been dealing other drugs, or they have committed vandalism. (These problematic behaviors are discussed in more detail in another section.)
3. Avoid allowing yourself to become upset during a confrontation. To do this, think through the interaction beforehand, and imagine yourself calmly addressing the problem with the patient. Anticipate their possible responses and what you will do.
4. If indicated, when confronting the patient make sure to include statements that you are concerned about the person's well-being and ultimate success in treatment.

Principle #8

Employ constant monitoring

Check urine, breath tests regularly

Provides early detection of use

Provides structure and external control (which some patients find helpful when deciding to not use)

1. It can be useful to explain to the patient at the start of treatment that a routine part of your practice is to monitor all patients through use of various tests relevant to their particular condition (such as urine testing for opioids – and blood testing of sugar in diabetics, and blood pressure checks in people with high blood pressure).

Principle #9

Take advantage of all resources in your area

Be familiar with resources in the area, and be ready to use them when needed

Resources can include residential services, partial hospitalizations programs, intensive outpatient, groups

1. These were reviewed earlier in the Role of Non-pharmacological Treatments section.
2. Get familiar with resources in the community and be ready to use them when needed.

Principle #10

Provide for a variety of treatment interventions

Pharmacotherapy alone is rarely sufficient for achievement of treatment stability

Since some community-based programs discourage use of medications, choose programs with care

1. Not only is it good and useful to know what resources are available in the community, but you should be familiar with them – for example, their philosophical approaches, their staffing, etc.

Principle #11

Enlist the assistance of recovering substance abusers

Can provide role models for the patient

Can be found through a call to the General Service
Office of AA/NA

1. If the patient is attending AA or NA, encourage them to obtain a sponsor and a home group.
2. If you have patients in treatment who have been doing well for one or two years (or more) and want to help others, consider exploring with them a role as a resource for new patients entering treatment. (However, patients early in treatment – for example, less than 1-2 years – should generally not be asked to take on such a role. Clinical experience suggests early recovery is a time for patients to focus on their own achievement of treatment stability, and not expend energy in attempting to assist others.)

Principle #12

Explore counseling or psychotherapy

This is an important element in the general management of substance abusers

Refer until a good match occurs with therapist/counselor and therapy

Can aid with issues not addressed in 12 step programs or with a recovering sponsor

1. If the patient enters into treatment with a counselor or therapist elsewhere, make sure your treatment is coordinated with that treatment. Keep up to date on the patient's progress, make sure you're consulted if medications are considered or started, and periodically let the counselor or therapist know how your treatment is progressing.
2. Similarly, coordinate the treatment for medical services. Be vigilant about new medications prescribed by other physicians – especially medications that could be abused (e.g., for sleep, or pain). Monitor as well for medications that can interfere with buprenorphine.

Principle #13

Review general health measures

Identify and treat, or refer for treatment medical and surgical problems

Review diet and exercise

1. Be aware of the patient's overall health status. Counsel appropriately. Assess and monitor for other problematic behaviors – such as smoking, gambling, excessive use of alcohol. Provide primary health care or refer for treatment as needed.

Principle #14

Educate the patient about psychoactive drugs and their effects

Can be accomplished in groups, with written materials, as well as one on one

1. Especially when patients first enter treatment, provide them with information about drugs and their effects – both psychological and physical.

Principle #15

Review the treatment plan regularly

Are adjustments indicated

In the frequency of office visits

In the frequency of urine testing

In dosage of medication

In the treatment goals

1. Once a sustained period of abstinence is achieved, other issues in the person's life may need to be addressed in order to achieve treatment stability. Other issues can include problems that are physical (a failure to have attended to basic health care during years of substance use), psychological (demoralization with lost opportunities), and interpersonal (relationships that have been strained or broken). While many of these sorts of problems should not be the primary focus of treatment when a person is actively abusing substances, once abstinence is maintained then it is appropriate to address them.

2. For patients who feel overwhelmed with their problems, it can be useful to point out that many others have been in similar situations, and have successfully moved on with their lives and regained much that they thought was lost. They are not the first person to be in the spot they now find themselves. Reassure them that successes in life can be accomplished, and that resources are available to help them achieve this.

Principle #16

The goals of treatment need to be defined

Cessation (versus reduction) of illicit opioid use

Cessation of all non-medically supervised psychoactive substance use

The importance of treatment stability

1. As discussed at the beginning of this talk, the practitioner will need to decide his/her goal of office-based treatment with buprenorphine. It is recognized that there can be differences of opinion about the proper goal of substance abuse treatment. Some believe that reductions in heroin use, for example, are an appropriate goal (since risk of acquiring infectious diseases is then reduced). Others believe that cessation of all illicit opioid use should be the goal, but point out that buprenorphine treatment is not meant to address other substance use such as cocaine, cannabis, or benzodiazepine abuse. Yet others maintain that patient well-being can only be improved when cessation of all non-medically supervised substance use has occurred.

2. It would seem that the physician who fails to address sporadic heroin use (or other opioid use that is occurring through illegal means), or other substance use (such as cocaine use), is failing to adequately treat the patient. If treatment stability is accepted as an appropriate goal, then efforts should be made to end the patient's inappropriate, non-medically supervised use of substances, and to address those aspects of the patient's life that have been adversely effected by their substance use. Non-pharmacological interventions can be used to help achieve this treatment stability.

Summary

Non-pharmacological treatment is an important and necessary part of office-based buprenorphine treatment

Understanding principles of non-pharmacological treatment for substance abuse can help the clinician in treating the buprenorphine-maintained patient

These principles emphasize the roles of structure, monitoring, and coordination when treating opioid-dependent patients in the office

Psychiatric Co-Morbidities

Psychiatric Co-Morbidities (Dual Diagnosis)

The purpose of this section is to review the core features of psychiatric conditions that commonly occur in patients with opioid dependence.

It is important for the practitioner who uses office-based buprenorphine to be familiar with these disorders because psychiatric co-morbidity is common in opioid dependent patients, and these disorders can complicate the successful treatment of patients.

1. This section covers psychiatric disorders that co-exist fairly commonly with opioid dependence (as well as other substance abuse disorders). Both illnesses (e.g., major depression) and symptoms (e.g., suicidal ideation) are covered in this section.

This section does not review other co-morbid substance use disorders (such as cocaine, alcohol, etc.), which are also commonly found in patients with opioid dependence. However, concurrent substance use can complicate the assessment of psychiatric symptoms, and recognizing the complicated association between substance use and psychiatric symptoms is important in the assessment and treatment of opioid dependent patients.

1. This section focuses on opioid dependence and concurrent psychiatric diagnoses – it does not review co-existing substance use disorders such as cocaine or alcohol abuse and dependence.
2. Symptoms of psychiatric disorders are common in patients who are abusing opioids. Concurrent use/abuse can complicate the assessment of psychiatric symptoms. As noted in the Guidelines, “Substance use and addiction can mimic, exacerbate, or precipitate psychiatric symptoms and disorders. Most substances of abuse produce moderate to severe psychiatric symptoms, and there is a complex association between substance abuse and psychiatric status.”

Outline for This Talk

- I. Epidemiology
- II. Psychiatric assessment and co-morbidities
- III. Treatment principles
- IV. Summary

1. There are three topics covered in this talk.

Outline for This Talk

- I. Epidemiology
- II. Psychiatric assessment and co-morbidities
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- IV. Summary

1. We'll begin with the first section, which reviews the epidemiology of co-morbid psychiatric disorders.

Epidemiology of Psychiatric Co-Morbidity

Increased rates of psychiatric disorders among opioid abusers

Reported rates can vary depending on population studied (e.g., demographics, treatment seeking)

Most common disorders: Major Depression, Anxiety Disorders, Personality Disorders

1. Numerous studies have assessed opioid dependent patients and shown high rates of co-morbid psychiatric disorders.
2. Note that studies have typically assessed patients seeking treatment for opioid dependence. No studies have examined a large population of opioid dependent persons in the community (non-treatment seeking), to determine rates of co-morbid disorders. Thus, these rates represent a selected sample.
3. There is considerable range in reported rates of disorders (as we will see on following slides). This may reflect differences in demographics of study populations. For example, a sample that has no women may have lower overall rates of depression and higher rates of antisocial personality disorder, versus a mixed gender sample.
4. Variability may also reflect the use of different assessment instruments, the type of treatment being sought, and the area of the country.

[References:

Rounsaville B.J., Weissman M.M., Kleber H.D., Wilber C. Heterogeneity of psychiatric diagnosis in treated opiate addicts. *Arch Gen Psychiatry* 39:161-166, 1982.

Khantzian E.J., Treece C. DSM-III psychiatric diagnosis of narcotic addicts. *Arch Gen Psychiatry* 42:1067-1071, 1985.

Broner R.K., King V.L., Kidorf M.S., Schmidt C.W., Bigelow G.E. Psychiatric and substance use comorbidity among treatment-seeking opioid abusers. *Arch Gen Psychiatry* 54:71-80, 1997.]

Epidemiology of Psychiatric Co-Morbidity

Major depression

Depressive symptoms are common for many patients at time of treatment entry, and frequently resolve as patient engages in treatment

Lifetime rates: 15-50%

Current rates: 3-25%

1. Symptoms of major depression (which is also called Unipolar Disorder) are very common in opioid dependent patients seeking methadone treatment. Notably, such symptoms resolve in the majority of patients within the first few days and weeks of treatment. Thus, they probably represent a level of general distress for the patient, rather than a major depression.
2. The wide range in current rates of major depression may reflect the time of assessment of patients. In studies where patients are initially stabilized on methadone, then assessed for depression, current rates tend to be quite low (<5%; Brooner et al., 1997). However, as in the general population, there are differences in prevalence rates for men versus women (with higher rates of major depression in populations of opioid-dependent women versus men).

[References:

Kosten T.R., Rounsaville B.J., Kleber H.D. A 2.5-year follow-up of depression, life crises, and treatment effects on abstinence among opioid addicts. *Arch Gen Psychiatry* 43:733-738, 1986.

Rounsaville B.J., Weissman M.M., Crits-Christoph K., Wilber C., Kleber H.D. Diagnosis and symptoms of depression in opiate addicts. *Arch Gen Psychiatry* 39:151-156, 1982.

Woody G.E., O'Brien C.P., Rickels, K. Depression and anxiety in heroin addicts: A placebo-controlled study of doxepin in combination with methadone. *Am J Psychiatry* 132:447-450, 1975.

Brooner R.K., King V.L., Kidorf M.S., Schmidt C.W., Bigelow G.E. Psychiatric and substance use comorbidity among treatment-seeking opioid abusers. *Arch Gen Psychiatry* 54:71-80, 1997.]

Epidemiology of Psychiatric Co-Morbidity

Depression at the time of treatment entry has prognostic significance in opioid dependent patients

Follow up studies show higher rates of illicit drug use in patients who present with depressive symptoms

1. This was found in a study that did a follow up at 6 months (Rounsaville et al., 1982), as well as one that did a follow up at 2.5 years (Kosten et al., 1986).
2. However, note that these studies examined patients before stabilization in treatment – that is, when they first were entering treatment. Thus, the depressive symptoms noted may have resolved within the first weeks of treatment. This means the association noted may be between level of general distress at the time of treatment entry and subsequent drug use, rather than the presence of a major depressive episode.

Epidemiology of Psychiatric Co-Morbidity

Anxiety disorders

Most common disorders are phobias, followed by
Generalized Anxiety Disorder

Lifetime rates: 8-27%

Current rates: 5-17%

1. Note the rates on this slide are for all anxiety disorders combined. Like depressive symptoms, anxiety symptoms can overlap with other substance related problems (for example, alcohol withdrawal), and for some patients can resolve within the first few days or weeks of treatment.

2. Rates for phobias:

lifetime: 2-9%

current: not well studied, one report found 9% (Rounsaville et al., 1982)

3. Rates for Generalized Anxiety Disorder (GAD):

lifetime: up to 5%

current: about 1% (or less)

4. Rates for panic disorder:

lifetime: up to 2%

current: <1%

5. Rates for Obsessive Compulsive Disorder (OCD):

lifetime: <2%

current: 1%

Epidemiology of Psychiatric Co-Morbidity

Personality disorders

Highly prevalent in patients with opioid dependence

Most common of these is Antisocial Personality Disorder (APD), particularly in men

Rates (any personality disorder): 35-68%

Rates (APD): 14-55%

[References:

Woody G.E., McLellan A.T., Luborsky L., O'Brien C.P. Sociopathy and psychotherapy outcome. *Arch Gen Psychiatry* 42:1081-1086, 1985.

Kosten T.R., Rounsaville B.J., Kleber H.D. DSM-III personality disorders in opiate addicts. *Comp Psychiatry* 23:572-581, 1982.]

Epidemiology of Psychiatric Co-Morbidity

Other psychiatric disorders

Schizophrenia: Relatively rare

Bipolar disorder: Less common than major depression (unipolar disorder)

Eating disorders: Lifetime history not uncommon, but rarer to be a current problem

Attention Deficit Hyperactivity Disorder (ADHD):
Considerable interest, but little information about prevalence

1. Schizophrenia may be occasionally seen in opioid dependent patients, but there does not appear to be an increased rate of schizophrenia among opioid dependent persons (relative to the general population).
2. Bipolar disorder is less commonly seen than major depression (which is also known as unipolar disorder) in patients with opioid dependence.
3. A history of eating disorders may be reported in opioid dependent patients (especially women), but current eating disorder problems are rare.
3. While some reports have suggested ADHD may be common in substance abuse patients, not all studies have shown this to be the case. Diagnosing ADHD in adults with substance abuse disorders can be difficult. In order to obtain accurate, valid reports of childhood behaviors, history from collateral sources (such as parents and/or school records) should be collected.
4. Other co-morbid psychiatric disorders in opioid dependent patients that have been reported include pathological gambling and post-traumatic stress disorder (PTSD). While these disorders may be more common in this population, there is little work on their prevalence.

[References:

King V.L., Brooner R.K., Kidorf M.S., Stoller K.B., Mirsky A.F. Attention deficit hyperactivity disorder and treatment outcome in opioid abusers entering treatment. *J Nerv Ment Dis* 187:487-95, 1999.

Levin F.R., Evans S.M., Kleber H.D. Prevalence of adult attention-deficit hyperactivity disorder among cocaine abusers seeking treatment. *Drug Alcohol Depend* 52:15-25, 1998.]

Outline for This Talk

I. Epidemiology

II. Psychiatric assessment and co-morbidities

III. Treatment principles

IV. Summary

Psychiatric Assessment

Overview

Features of co-morbid disorders

Substance-induced versus independent disorders

Areas to assess

1. In this section on psychiatric assessment, there are four topics to be covered. We'll begin with an overview to assessments.
2. Assessment is the beginning of the therapeutic process. The clinician's interest in psychiatric and social issues during the time of the assessment can help foster a therapeutic alliance and can increase the likelihood that the patient will engage successfully in treatment.

Psychiatric Assessment – Overview

Assessments can be done by interview or with questionnaires

Interview can result in diagnoses, but takes time and effort

Questionnaires assess symptoms, don't diagnose

Interviewer-based assessment provides opportunity to begin therapeutic process

1. Tools for psychiatric assessments fall into two broad categories – interviews and questionnaires.
2. Interviews can include both structured interviews – like the Structured Clinical Interview for DSM-IV, or SCID – as well as unstructured clinical interviews. Interviews are time intensive and require specialized training for the interviewer.
3. Questionnaires are more time efficient for the treatment staff than interviews, but don't provide diagnoses. Furthermore, the validity of the patient's responses aren't typically assessed. There are numerous questionnaires used in psychiatric assessments for things like depression (the Beck Depression Inventory), anxiety (the State-Trait Anxiety Inventory), and personality (the NEO-PI). Questionnaires can be an effective tool for screening patients. Positive responses can then be followed up in an interview.

[References:

First M.B., Spitzer R.L., Gibbon M., Williams J.B.W. Structured Clinical Interview for DSM-IV Axis I Disorders -- Patient Edition (SCID-I/P, Version 2.0). Biometrics Research Department, New York State Psychiatric Institute, New York, NY 10032, 1995.

Costa P.T., McCrae R.R. The NEO Personality Inventory Manual. Psychological Assessment Resources, Odessa, FL, 1985.

Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 4:53-63, 1961.]

Psychiatric Assessment – Overview

Should focus assessment on particular areas where high likelihood of co-morbid disorders and potential for problematic symptoms

If using questionnaires, then need to look at results and follow up with face-to-face evaluation of patient by the physician

Full psychiatric assessment may require more than one visit to complete

1. The full psychiatric assessment should be considered for some patients. The assessment may require more time than is available during a single office visit, and can be spread out over multiple visits if needed. For the non-psychiatrist, referral to a psychiatrist should be made for a full psychiatric assessment.
2. A full psychiatric assessment should be considered for patients who present with a history of psychiatric treatment (either inpatient or outpatient), or who report high levels of psychiatric symptoms (such as depression, anxiety, or false perceptions and/or beliefs such as hallucinations and delusions). Patients who have highly unstable lives – especially if the instability seems independent of their substance abuse – may also need a full psychiatric assessment.

Psychiatric Assessment

Overview

Features of co-morbid disorders

Substance-induced versus independent disorders

Areas to assess

1. Before discussing further the assessment for psychiatric disorders, this section will review the features of these disorders.

Psychiatric Assessment – Features of Disorders

Major depression

Anxiety disorders

 Phobias

 Generalized anxiety disorder

Personality disorders

 Antisocial personality disorder

Opioid intoxication and withdrawal

1. Specifically, this section reviews the diagnostic features of the major psychiatric disorders that frequently co-exist with opioid dependence.
2. In addition, this section also reviews the signs and symptoms of opioid intoxication and withdrawal, since their symptomatic presentation can overlap with these other psychiatric disorders.

[Reference:

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). American Psychiatric Association, Washington, D.C., 1994.]

Psychiatric Assessment – Features of Disorders

Major depression

Depressed mood

Anhedonia

Weight/appetite change

Sleep change

Psychomotor agitation/retardation

1. The primary feature of a Major Depression (or “Major Depressive Disorder” as it is called in DSM-IV), is either a depressed mood or a loss of pleasure or interest (anhedonia) that is sustained over a period of time (typically two or more weeks). Other features of Major Depression are shown on this and the next slide.
2. A person does not need to have all these features to fulfill the criteria for Major Depression. In DSM-IV there are nine criteria (shown here), and the person must have five of the nine (with at least one being either depressed mood or anhedonia).
3. Note that Major Depression is not diagnosed if the symptoms are due to the physiological effects of a substance, or if the symptoms are better accounted for by grieving (Bereavement).

Psychiatric Assessment – Features of Disorders

Major depression (continued)

Loss of energy

Feeling worthless/inappropriate guilt

Decreased concentration

Thoughts of death/suicidal ideation

1. We will talk more about suicidal ideation later in this section, but a couple of comments are worth making here.
2. First, asking a patient about suicidal ideation does not increase their risk of having such thoughts – it isn't that a seed is planted in their mind by your asking. It is better to ask than to not ask.
3. It is also good to ask about a desire to die (not simply a desire to commit suicide). Some depressed people report they don't want to kill themselves (for example, because it is a sin), but they would welcome death (a "passive death wish").

Psychiatric Assessment – Features of Disorders

Anxiety disorders: Phobias

Excessive and unreasonable fear

Can be of an object (animal), situation (flying),
social/performance event (eating)

Exposure produces intense anxiety/distress

Avoidance

1. There are three types of phobias:
 - a. Specific phobias: excessive or unreasonable fear of objects or situations (for example, blood, flying, heights, animals, needles)
 - b. Social phobias: fear of social or performance situations (for example, eating in front of others, public speaking)
 - c. Agoraphobia: fear of places or situations where the person might not be able to escape without difficulty or embarrassment (for example, being in crowds or on elevators) – especially if sudden anxiety symptoms should develop; note that according to DSM-IV only agoraphobia is coded as being either with or without panic disorder

Psychiatric Assessment – Features of Disorders

Anxiety disorders: Generalized anxiety disorder

Excessive anxiety and worry, difficult to control

Restlessness/feeling keyed up

Easy fatigue

Difficulty concentrating

1. To meet the criteria for a diagnosis of GAD, symptoms must occur more days than not, for at least 6 months.
2. Patients may present with prominent anxiety symptoms at that time of treatment entry. Studies have not assessed the time course and resolution of such anxiety symptoms as patients stabilize in treatment. However, clinical experience suggests that for many patients there is a resolution of anxiety symptoms as they stabilize in treatment.

Psychiatric Assessment – Features of Disorders

Anxiety disorders: Generalized anxiety disorder
(continued)

Irritability

Muscle tension

Sleep disturbance

Psychiatric Assessment – Features of Disorders

Personality disorders

No single defining feature to these conditions – a heterogeneous grouping

Personality characteristics are things we all have (e.g., introversion, conscientiousness)

Personality disorders are extremes in these common features

Enduring patterns of functioning that are problematic

1. Everyone has personality characteristics – features that vary along a dimension (such as introversion/extroversion and conscientiousness). There are numerous such dimensions of personality.
2. People with personality disorders fall on the extremes of such dimensions.

It's important to note that we tend to look at people's behavior to characterize their personality, but that not all behavior grows out of personality. With respect to drug abuse, some patients will engage in contra-social behavior (lying, stealing) in order to support their drug use. While we may think of them as being antisocial, in actuality this contra-social behavior stops once their drug use stops.

Psychiatric Assessment – Features of Disorders

Personality disorders: Antisocial personality disorder

Features begin in childhood (Conduct Disorder)

Repeatedly breaking the law

Lying/conning

Impulsivity

Physical fights

1. Antisocial Personality Disorder falls in a cluster of personality disorders that include Borderline, Narcissistic, and Histrionic personality disorders (“Cluster B”). It is more common in men than women. Note that often patients can fulfill DSM-IV criteria for more than one personality disorder – for example, both APD and Borderline personality disorder.

Psychiatric Assessment – Features of Disorders

Personality disorders: Antisocial personality disorder (continued)

Disregard for safety of self, others

Consistent irresponsibility

Lack of remorse

Psychiatric Assessment – Features of Disorders

Opioid intoxication and withdrawal

It is important to recognize and distinguish symptoms of opioid intoxication and withdrawal, since their symptomatic presentations can overlap with the signs and symptoms of other psychiatric disorders.

- 1.

Psychiatric Assessment – Features of Disorders

Opioid intoxication

Occurs shortly after use of an opioid

Effects vary depending upon whether the person is physically dependent (versus not dependent but with a history of use, or no history of use), level of dependence, dose of opioid used, route of administration

1. Opioid intoxication effects can vary in three different populations. Those who are: (1) physically dependent, (2) not physically dependent but have a history of abusing opioids, and (3) not physically dependent and experimenting with opioids for the first time.
2. In the physically dependent, acute effects may be minimal (and use may primarily address relief of withdrawal).
3. In the non-physically dependent with a history of abuse, acute effects may be euphoria and other effects we'll see on the next slide.
4. Finally, in the person who has never used opioids before, the effects can also be like those seen in the person with a history of abuse (but not physically dependent). However, they may also report more of a sick feeling associated with their first use of opioids. Some people with opioid abuse or dependence report in retrospect that this was a “pleasant sick” – for example, they felt ill, vomited, then felt good or high.

Psychiatric Assessment – Features of Disorders

Opioid intoxication

Signs and symptoms:

Feeling of “high” or euphoria

Pupillary constriction

Drowsiness or coma

Slurred speech

Impaired attention or memory

1. A person doesn't necessarily have all these features when intoxicated with opioids.
2. The feeling of euphoria can progress to a feeling of dysphoria or apathy.
3. A person can overdose with opioids, develop respiratory depression, and become anoxic (and die). If anoxia is present, then pupillary dilation rather than constriction will occur.

Psychiatric Assessment – Features of Disorders

Opioid withdrawal

Occurs after stopping or decreasing use that has been occurring regularly (e.g., daily for weeks) – this is spontaneous withdrawal

Note it can also occur if person receives a dose of an opioid antagonist or partial agonist – this is precipitated withdrawal

1. The severity, onset and duration of spontaneous opioid withdrawal depends upon the type of opioid being used and the amount being used (the level of dependence). For people dependent on heroin, onset usually begins 8-12 hours after the last dose, peaks at 36-72 hours, and resolves by 5 days.
2. Precipitated withdrawal begins quickly (it can occur minutes after the injection of an antagonist). The duration depends upon the antagonist used – for naloxone, it can be relatively short (45-90 minutes), while for naltrexone it can last much longer (more than a day).
3. For a partial agonist (like buprenorphine) that is injected, precipitated withdrawal can have a relatively rapid onset (within the first hour after injection), relatively mild intensity, and duration that can last several hours. The likelihood of precipitated withdrawal by buprenorphine increases if the person has a high level of physical dependence (e.g., daily use of opioids equivalent to 60+ mg per day of methadone).
4. Note that if the combination of buprenorphine/naloxone were injected by an opioid dependent person, it is likely the antagonist effects of naloxone would produce a precipitated withdrawal syndrome of greater severity than the partial agonist effects of buprenorphine.

Psychiatric Assessment – Features of Disorders

Opioid withdrawal

Signs and symptoms:

- Dysphoric mood
- Nausea or vomiting
- Muscle aches/cramps
- Lacrimation
- Rhinorrhea

1. Opioid withdrawal is a very well characterized withdrawal syndrome.
2. Not all features listed on this and the next slide necessarily occur when a person is in opioid withdrawal.

Psychiatric Assessment – Features of Disorders

Opioid withdrawal (continued)

- Pupillary dilation
- Sweating, piloerection
- Diarrhea
- Yawning
- Fever
- Insomnia

1. As can be seen in these lists of signs and symptoms of opioid intoxication and withdrawal, patients can report feeling alterations in mood, sleep and appetite (for example) that are due to opioid use. However, these symptoms may be mistakenly attributed to a different psychiatric disorder. It is important for the clinician to recognize this overlap between signs and symptoms of opioid intoxication and withdrawal, and other psychiatric disorders, so that proper diagnosis and treatment can be made.

Psychiatric Assessment

Overview

Features of co-morbid disorders

Substance-induced versus independent disorders

Areas to assess

Psychiatric Assessment – Induced, Independent

Distinguish between substance-induced disorders versus independent psychiatric disorders

Substance-induced: Disorders related to the use of psychoactive substance; typically resolve with sustained abstinence

Independent: Disorders which present during times of abstinence; symptoms not related to use of psychoactive substance

1. This distinction has been made by using other terms as well, such as primary versus secondary disorders and major versus minor disorders.
2. Examples of substance-induced disorders include substance-induced mood disorders, substance-induced anxiety disorders, and substance-induced sleep disorders.

Psychiatric Assessment – Induced

Substance-induced disorders

Patient's history suggests symptoms occur only when he/she is actively abusing drugs

Symptoms are related to intoxication, withdrawal, or other aspects of active use

Onset and/or offset of symptoms are preceded by increases or decreases in substance use

Goal should be sustained abstinence followed by re-evaluation of symptoms

1. If the patient's history shows evidence of prior episodes of the same disorder that occur independent of substance abuse, then the current episode should not be considered substance-induced.
2. If a patient has experienced a sustained period of abstinence, while incarcerated, for example, it can be useful to probe for information about their mood and functioning during such a period of abstinence.
3. The patient may report opioid abstinence for a sustained period in the past, but still have psychiatric symptoms – for example, of depression. It is important to make sure that other drug or problematic alcohol use did not occur during such a time.

Psychiatric Assessment – Independent

Independent disorders

Patient's history suggests symptoms occur during periods when not using or abusing psychoactive substances, or during periods of steady use without change in amount or type

May also find a family history of the disorder

Goal of substance abuse treatment should still be cessation of substance use, but treatment may also address psychiatric symptoms simultaneously

1. With patients who have a clear history of an independent psychiatric disorder, a lower threshold for use of psychotropic medications should be employed. At the same time, the clinician should avoid allowing the patient to believe that treatment of a non-substance use disorder, such as depression, is all that is necessary to treat the substance abuse. The focus should also continue on their drug use.
2. Studies using antidepressant medications in the treatment of patients with substance abuse and an independent major depression have shown these medications can be effective.
3. The selection of a particular antidepressant medication should be guided by possible interactions with other medications the patient is taking (e.g., fluoxetine is an inhibitor of P450 3A4), the abuse liability of the antidepressant (some tricyclics with significant anticholinergic effects, such as amitriptyline, can be abused by some patients), and the patient's past response to antidepressants.

[Reference:

Nunes E.V., Quitkin F.M., Donovan S.J., Deliyannides D., Ocepek-Welikson K., Koenig T., Brady R., McGrath P.J., Woody G. Imipramine treatment of opiate-dependent patients with depressive disorders: a placebo-controlled trial. Arch Gen Psychiatry 55:153-160, 1998.]

Psychiatric Assessment

Overview

Features of co-morbid disorders

Substance-induced versus independent disorders

Areas to assess

Psychiatric Assessment

Areas that should focus on:

Depressive, anxiety symptoms

Personality

Suicide and homicide risk

Psychiatric Assessment – Areas to Assess

Depressive and anxiety symptoms

Common for opioid dependent patients to report high rates of depressive and anxiety symptoms at time of treatment entry

Symptoms often resolve within few days after entry (i.e., substance-induced)

1. Since patients often report depressive and anxiety symptoms upon entering opioid dependence treatment, the clinician may wish to follow these symptoms and re-assess them over the first few days and weeks of treatment to determine if they represent an independent disorder or a substance-induced disorder, before initiating treatment.
2. If the patient is reporting suicidal or homicidal ideation, then addressing this cannot be delayed. This topic will be covered later in this talk.
3. If there is evidence of an independent disorder, then pharmacological and non-pharmacological treatments may be initiated earlier rather than waiting these first days and weeks.

Psychiatric Assessment – Areas to Assess

Personality

Distinguish between behaviors that occur as part of drug use lifestyle versus personality disorder

Recognize limitations to treatment in office base

Refer to specialized services once cessation of illicit substance use achieved, if patient is distressed

1. Like other psychiatric disorders, optimal assessment of personality occurs when the patient has achieved a period of sustained abstinence.
2. For the non-psychiatrist providing office-based buprenorphine treatment, management and treatment of personality disorders may be particularly difficult and time consuming. Referral to psychiatric services should be considered.
3. Patients with personality disorders – especially antisocial personality disorder – may require a treatment team for structure and limit setting. A setting such as methadone maintenance may be better equipped to treat such patients.

Psychiatric Assessment – Areas to Assess

Personality

Personality disorders represent extremes in features that all people have

For example, patients may show extremes in impulse control, affective lability, actions in interpersonal relationships

Symptoms need to be enduring

1. Assessing for personality disorders can seem difficult at times. They are best diagnosed as the clinician gets to know the patient – a single visit or two can raise suspicion that a personality disorder is present, but getting to know the patient over time allows the clinician to have the best perspective on the patient's personality.
2. The clinician should consider areas of the patient's beliefs, samples of the patient's actions, and observations of the patient's emotions, when considering a diagnosis of a personality disorder. Patients who have achieved cessation of illicit drug use, but show evidence of a labile affect, difficulty in relationships, and/or unusual ideas or beliefs may have a personality disorder (or another psychiatric disorder). Assessment can include a review of criteria for categories of personality disorders (such as can be found in DSM-IV) or assessment of personality dimensions with questionnaires for personality (such as the NEO-PI).

Psychiatric Assessment – Areas to Assess

Suicide and homicide risk

Increased risk in substance abuse populations

Should ask about thoughts to harm self or others

Be prepared if answer is positive

1. Note that suicidal ideation is not specific for any particular psychiatric disorder. It can be seen in patients with substance abuse, depression, schizophrenia, anxiety disorders, and personality disorders.
2. Note that suicidal intent and lethality can be independent: patients with low intent can commit highly lethal acts.
3. Consider referral to an emergency department (ED) for psychiatric evaluation and/or admission if it appears the patient is at risk for harming self or others, or if you are not familiar and comfortable with assessing suicidal or homicidal ideation. Consider legal intervention (e.g., an emergency petition) if the patient is unwilling to go to the ED.
4. If need to refer patient to ED, reassure the patient that you will arrange for opioid dependence treatment (and do so).
5. If weapons are available to the person, contact a family member and have the weapons removed from the home.
6. Don't discharge the patient from treatment simply because they have evidence of suicidal or homicidal ideation.

Psychiatric Assessment – Areas to Assess

Suicide risk increased by

Prior suicide attempt

Greater suicidal preoccupation

Level of intent and formulation of plan

Availability of lethal means

Psychiatric Assessment – Areas to Assess

Suicide risk increased by (continued)

Family history of completed suicide

Presence of active mental illness

Current negative life events

Serious medical illness

Active substance abuse

Psychiatric Assessment – Areas to Assess

Suicide assessment

Determine level of intent (low-high)

Ask if there is a plan (patient has written a note to others about suicide plan; level of lethality for the plan)

Identify if reasons to not harm self (family, getting treatment for substance abuse)

1. It is useful to distinguish suicidal ideation from self-injurious behavior (SIB). Some patients with severe personality disorders (Borderline, Histrionic) may engage in SIB – cutting their bodies, for example. This is not necessarily a suicide attempt in such patients – although it is important to note that such behavior can kill. The patient's level of intent to die may be extremely low. However, the lethality can be high despite low intent. Thus, assessment of the suicidal patient should include an evaluation of both level of intent and lethality of plan.

Psychiatric Assessment – Areas to Assess

Suicide assessment (continued)

Accessibility of the means, if present

If the desire is active (wants to kill self) or passive
(doesn't want to kill self, but would welcome death)

If there is a past history of suicide attempts

If there is a family history of suicide

1. Be prepared if the patient reports suicidal ideation, and conduct a further assessment. To summarize areas that should be assessed:
 - a) the strength of the intent
 - b) if there is a means planned
 - c) the lethality of the means, if present
 - d) whether the person has written a note
 - e) if there are reasons for the person to live (e.g., children)
 - f) if the desire is active (wants to kill self) or passive (doesn't want to kill self, but would welcome death)
 - g) if there is a past history of suicide attempts
 - h) if there is a family history of suicide

Psychiatric Assessment – Areas to Assess

Homicide risk

Is there an identifiable person threatened?

Is the threatened person aware?

Access to weapons?

1. If the patient wishes to harm a specific person, then a warning should be made to that person (in addition to the police in most circumstances). In addition, the patient may be best served with psychiatric hospitalization for further evaluation.
2. If weapons are available to the patient, then contact a family member and ask him/her to remove the weapons from the home.

Outline for This Talk

- I. Epidemiology
- II. Psychiatric assessment and co-morbidities
- III. Treatment principles**
- IV. Summary

Treatment Principles

General principles of treatment

Depression and anxiety

Personality disorders

Suicidal and homicidal ideation

Treatment Principles – General Principles

For unclear cases (e.g., no prior clear documentation of an independent episode), ensure period of abstinence from drug and alcohol use prior to diagnosis

Evaluate for co-morbid medical problems that might cause psychiatric symptoms

People who respond to treatment are those who want help (are in distress)

Consider referral if patient needs further evaluation or treatment of co-morbid psychiatric disorders

1. The amount of time a person should be abstinent before diagnosing a co-morbid psychiatric disorder can vary depending upon the circumstances of the patient, his/her history, and the types of drugs used. In general, substance-induced depressive symptoms in opioid dependent patients begin to decline within the first week of treatment and are substantially reduced within the first month. Similar patterns of resolution over time occur in patients using other drugs. For example, substance-induced depressive symptoms resolve within the first and second week of treatment for alcohol dependent patients. However, some clinicians believe that patients can have “protracted withdrawal” from substances – that is, withdrawal symptoms (perhaps most commonly complaints of sleep disturbance) that persist for months.
2. If the patient has evidence of severe psychiatric symptoms (e.g., delusions, hallucinations, profound depression with suicidal ideation), then stabilization of these symptoms should occur before initiating office-based buprenorphine treatment. Such stabilization may require inpatient psychiatric treatment.
3. Less severe psychiatric symptoms at the time of presentation may be followed and re-assessed by the office-based physician, while starting the patient on buprenorphine. Resolution of symptoms may occur with stabilization in treatment. Sustained symptoms may be addressed once treatment stability is achieved, either as part of the office-based treatment (if the physician is experienced and comfortable in doing so), or referral to a psychiatrist or mental health care clinic.

Treatment Principles

General principles of treatment

Depression and anxiety

Personality disorders

Suicidal and homicidal ideation

Treatment Principles – Depression, Anxiety

Patients with opioid dependence and independent depressive and anxiety disorders can respond to medication treatments for depressive and anxiety conditions (similar to the general population)

Generally avoid use of benzodiazepines, since risk of abuse and possibility of interactions with buprenorphine

1. Studies of medications for the treatment of independent major depression in opioid dependent patients have been primarily with tricyclic antidepressants (TCAs). These studies have shown that patients respond with improvement in their depression. It seems likely that use of SSRIs would also be effective in this circumstance, although similar well controlled studies have not been conducted.
2. Pharmacological treatments for anxiety disorders should begin with non-benzodiazepine medications (e.g., buspirone, SSRIs, TCAs). Benzodiazepines can be abused by opioid-dependent patients, and use of these medications can become complicated due to problems such as diversion and extra dosing. In addition, reports of respiratory depression and death associated with the combination of a benzodiazepine and buprenorphine have appeared in the scientific literature (from experience with buprenorphine in France).
3. Abused benzodiazepines tend to have rapid onsets of action and shorter half-lives. Avoid use of short-acting benzodiazepines (e.g., alprazolam, clonazepam). Consider very carefully if contemplating use of a benzodiazepine in a buprenorphine maintained patient (because of the respiratory depression risk), and consider obtaining a second opinion on management of the patient's anxiety. If, after careful consideration and consultation, it is decided a benzodiazepine must be prescribed, use a low abuse potential, long-acting benzodiazepine such as oxazepam, and caution the patient appropriately.

[Reference:

Nunes E.V., Quitkin F.M., Donovan S.J., Deliyannides D., Ocepek-Welikson K., Koenig T., Brady R., McGrath P.J., Woody G. Imipramine treatment of opiate-dependent patients with depressive disorders. A placebo-controlled trial. Arch Gen Psychiatry 55:153-60, 1998.]

Treatment Principles – Depression, Anxiety

Don't overlook importance of non-pharmacological approaches to treatment (e.g., cognitive-behavioral therapy), especially in patients with mild/moderate anxiety

1. Non-pharmacological treatments can also be effective in the treatment of depression.

Treatment Principles

General principles of treatment

Depression and anxiety

Personality disorders

Suicidal and homicidal ideation

Treatment Principles – Personality

Can be difficult to treat conditions (especially severe personality disorders such as Borderline, Narcissistic, Histrionic, Antisocial)

Consider referral to specialized services

Severity of personality vulnerabilities and associated maladaptive behaviors often decline with cessation of substance use

Treatment Principles

General principles of treatment

Depression and anxiety

Personality disorders

Suicidal and homicidal ideation

Treatment Principles – Suicidal Ideation

Assess level of intent, level of lethality, risk factors

Consider referral to emergency services (crisis service, emergency department)

Recognize low intent patients can have high lethality attempts

Treatment Principles – Homicidal Ideation

Determine if patient has insight into consequences of possible actions

Consider duty to warn threatened person

May need referral to emergency services

Outline for This Talk

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Summary

Psychiatric co-morbidity is common in opioid dependent patients

Assessment is complicated by overlap between substance-related symptoms and independent disorders

Referral to specialized services may be useful

Treatment of both substance abuse and co-morbid psychiatric disorder essential to achieve treatment stability

Medical Co-Morbidity

Medical Co-Morbidity

Opioid-dependent patients who present for treatment often have other medical problems. These medical conditions are a consequence of both active and past high-risk behaviors, including injection drug use and the direct toxic effects of illicit drugs with a variety of active and inert additives. It is important for clinicians who treat opioid-dependent patients with buprenorphine to screen for and treat (or refer for treatment) common co-morbid medical conditions.

Office-based buprenorphine treatment provides the opportunity to integrate the delivery of substance abuse treatment, screening for these other co-morbid medical conditions, and their management. In addition, this setting allows the clinician to discuss appropriate preventive measures pertinent for this patient population.

The purpose of this section is to provide the clinician with an overview to the common co-morbid medical conditions found in opioid-dependent patients, and to review the features of preventive health care for these patients. It is important to know about these topics because integration of screening and treatment (or referral for treatment) of these co-morbid disorders with office-based buprenorphine will improve the health of patients being treated with buprenorphine.

Outline for This Talk

- I. Hepatitis B
- II. Hepatitis C
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- V. Preventive health care for opioid dependent patients
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1. This section reviews common co-morbid medical conditions found in patients with opioid dependence, and also provides a review of the preventive health care that should be followed in such patients.

2. Some of the most common co-morbid medical disorders in patients with opioid dependence are viral infections. Many of these infectious complications are the result of the process of injecting opioid substances. In one study, the prevalence of viral infections in injection drug users was:

<u>Infection</u>	<u>Seroprevalence</u>
HCV	77%
HBV	66%
HIV	21%
HTLV	22%

[Reference:

Garfein R.S., Vlahov D., Galai N., Doherty M.C., Nelson K.E. Viral infections in short-term injection drug users: the prevalence of the hepatitis C, hepatitis B, human immunodeficiency, and human T-lymphotropic viruses. Am J Public Health 86:655-61, 1996.]

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1. It is important to know about Hepatitis B (and these other medical conditions), even if the practitioner is not going to be treating patients for these disorders. Being familiar with these conditions will allow the clinician to understand the patient's overall health status, and to assist the patient in making informed decisions. In addition, it will help the patient if the clinician can advocate treatment for the patient, if the clinician does not provide that treatment directly.

Hepatitis B

Definition

Epidemiology

Clinical course

Treatment

Hepatitis B

Definition

Hepatitis B (HBV) is a blood-borne viral pathogen

Hepatitis B

Definition

Epidemiology

Clinical course

Treatment

Hepatitis B

Epidemiology

Estimated 1-1.25 million chronically infected in U.S.

Incidence: 140,000-320,000 per year in U.S.

Transmission by blood-borne (parenteral), sexual, or perinatal routes

Approximately 50% of active injecting drug users have serological evidence of prior exposure to HBV; majority show evidence of active viral infection

Hepatitis B

Definition

Epidemiology

Clinical course

Treatment

Hepatitis B

Clinical course

Early and mild viral hepatitis manifests with symptoms of hepatic inflammation and damage with elevated serum transaminases

Chronic viral hepatitis manifests as chronic liver disease with portal hypertension and poor hepatic synthetic function

1. During early viral hepatitis, serum transaminase levels can rise to 10-20x normal. Bilirubin and alkaline phosphatase will also likely be elevated.
2. Symptoms of acute hepatitis can include malaise, fatigue, anorexia, nausea, vomiting, myalgia and headache, along with arthritis, urticaria, and mild fever. The majority of patients make a full recovery (94%), but a minority of patients (5%) do develop chronic hepatitis (and 30-40% of those patients develop cirrhosis), and 1% develop fulminant hepatitis (with 80% of that 1% requiring liver transplantation).
3. Evidence of portal hypertension can include ascites, gynecomastia, and esophageal varices.
2. Evidence of poor hepatic synthetic function can include decreased albumin and elevated prothrombin time.

Hepatitis B

Clinical course (continued)

Patients with prior infection display one of two patterns:

Positive serology for Hepatitis B surface antibody,
and/or

Positive serology for Hepatitis B core antibody

1. Jaundice appears in only one-third of adult patients with acute hepatitis B.
2. Anti-HBc (IgM or IgG) is positive in all acute and chronic cases. It is a reliable marker of infection. Appearance begins relatively early after infection (between 1-2 months after infection).
3. Anti-HBs indicates convalescence from acute infection. Appearance begins 6 months after infection.
4. IgM anti-HBc represents active viral replication. It rises early in infection, and falls (and is lost) by 6-12 months after the onset of acute illness.
5. Unlike acute hepatitis B, patients with chronic hepatitis B have persistently high levels of HBsAg and HBeAg in the serum. Diagnosis is confirmed by HBV DNA in the serum or HBcAg in the liver.

Hepatitis B

Definition

Epidemiology

Clinical course

Treatment

Hepatitis B

Treatment

The goal of treatment is to halt progression of liver injury either by suppressing viral replication or by eliminating infection

Current treatment regimens for chronic hepatitis include Interferon-alpha and nucleoside analogues (e.g., Lamivudine)

1. Treatment of acute hepatitis is supportive therapy (e.g., rest, hydration, and adequate diet).

Hepatitis B

Treatment (continued)

Interferon is administered either as 5 million U subcutaneously qd or 10 million U subcutaneously three times per week, for 16 weeks

Meta-analysis of 16 randomized, controlled trials found loss of HBeAg and HBV DNA in 33-37% of interferon treated patients compared with 12-17% of controls

Hepatitis B

Treatment (continued)

Only 30-40% of selected patients achieve a sustained response

Hepatitis B

Treatment (continued)

The following factors predict a favorable response:

Low pretreatment HBV DNA

High serum transaminases

Female sex

Wild type virus

Shorter duration of hepatitis

Patients who do not meet these criteria have a response rate <5%

Hepatitis B

Treatment (continued)

Interferon side effects include:

Flu-like symptoms

Fatigue

Headache

Fever

Myalgias

Depression

1. Other side effects can include nausea, vomiting, and anorexia.
2. There are not studies examining the interaction of buprenorphine and interferon. However, there is some evidence that alpha-interferon can decrease the functioning of P450 enzymes, suggesting use of interferon with buprenorphine might decrease the metabolism of buprenorphine.

Hepatitis B

Treatment (continued)

Lamivudine, 100 mg per day, has yielded a serconversion response in nearly 33% of patients after one year; can be used in all patients with active viral replication

Efficacy of lamivudine limited by the development of resistance

1. There are no known interactions between lamivudine and buprenorphine, although there have not been systematic studies testing for such possible interactions.

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Hepatitis C

Definition

Epidemiology

Clinical course

Treatment

Hepatitis C

Definition

Hepatitis C (HCV) is a blood-borne viral pathogen previously called non-A, non-B hepatitis

Hepatitis C

Definition

Epidemiology

Clinical course

Treatment

Hepatitis C

Epidemiology

Incidence: 30,000 new cases per year in U.S.

Seroprevalence studies using second generation blood tests (ELISA) for Hepatitis C virus (HCV) antibody and testing for HCV-RNA reveal that between 0.3 and 1.2% of the general population are infected with HCV
HCV is more prevalent and more infectious than HIV

1. According to the CDC in 1999, there are 30,000 new cases of Hepatitis C in the U.S. each year.

Hepatitis C

Epidemiology (continued)

Greater than 90% of injection drug users have antibodies to HCV

Most transmission occurs by direct contact with infected blood and blood products, although may occur with sexual contact

1. Among patients infected with HCV, 75-85% do not have resolution but develop chronic HCV infection (elevated liver function tests and anti-HCV, or chronic hepatitis found upon liver biopsy). Patients with chronic hepatitis C often have few or no symptoms.

2. Risk factors for Hepatitis C:

<u>Risk Factor</u>	<u>Odds Ratio (95% CI)</u>
intravenous drug use	128 (26-625)
institutionalized	56 (11-276)
blood transfusion	11 (5-23)
sex with drug user	7 (3-15)
tattooing	6 (3-13)

[Reference:

Delage G., Infante-Rivard C., Chiavetta J.A., Willems B., Pi D., Fast M. Risk factors for acquisition of hepatitis C virus infection in blood donors: results of a case-control study. *Gastroenterology* 116:893-9, 1999.]

Hepatitis C

Epidemiology (continued)

In injection drug users, infection results from contact with contaminated needles, syringes, paraphernalia; blood and blood products are more infectious than saliva, vaginal secretions, or semen

Hepatitis C

Definition

Epidemiology

Clinical course

Treatment

Hepatitis C

Clinical course

Acute infection is followed by a 2-3 month lag period during which HCV antibodies are undetected

Clinical consequences of HCV infections occur in 80-85% of infected individuals

1. Risk factors for rapid progression of Hepatitis C are: infection at age <40 years; alcohol consumption >50 g/day; male gender.

Hepatitis C

Clinical course (continued)

Mean length of time between infection with HCV and:

Chronic hepatitis – 10 years

Cirrhosis – 20 years

Hepatocellular carcinoma – 30 years

1. Among patients with chronic hepatitis C, within the first 20 years after infection cirrhosis develops in at least 20%.
2. Risks factors for developing hepatocellular carcinoma are cirrhosis, advanced fibrosis (on liver biopsy), age, male sex, and alcohol abuse.

Hepatitis C

Clinical course: hepatitis

Symptoms:

50% of patients report symptoms including chronic fatigue and non-specific right upper quadrant abdominal discomfort

Serum transaminases:

Persistently elevated in 43%
Intermittently elevated in 42%
Normal in 15%

1.

Hepatitis C

Clinical course: cirrhosis, hepatocellular carcinoma

Cirrhosis develops in at least 20% of chronic carriers

Risk factors for disease progression include:

Alcohol use

Co-infection with Hepatitis B virus and/or HIV

Early onset infection (<40 years old)

Male sex

Hepatitis C

Definition

Epidemiology

Clinical course

Treatment

Hepatitis C

Treatment

Interferon plus ribavirin: sustained virologic response (absence of HCV RNA) following treatment with interferon, in addition to ribavirin, can occur in up to 40% of treated patients

Hepatitis C

Treatment (continued)

Interferon alone:

50% of patients normalize or reduce ALT by 50% or more

50% of those who respond suffer a relapse within 6 months

Hepatitis C

Treatment (continued)

Characteristics of those with a better response: not viral genotype 1; low level of viremia (HCV RNA); absence of cirrhosis

Longer treatment (6-12 months) may be more effective

Peginterferon alpha-2 has greater efficacy

1.

Hepatitis C

Treatment (continued)

Interferon side effects include:

Flu-like symptoms

Fatigue

Headache

Fever

Myalgias

Depression

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HIV/AIDS

Definition

Epidemiology

Clinical course

Treatment

HIV/AIDS

Definition

A blood-borne retroviral infection caused by the human immunodeficiency virus (HIV). Results in profound immunodeficiency related to destruction of CD4 lymphocytes which, in turn, leads to AIDS.

HIV/AIDS

Definition

Epidemiology

Clinical course

Treatment

HIV/AIDS

Epidemiology

Worldwide 30 million people infected with HIV

664,921 AIDS cases reported in U.S. through 1998

HIV-1 predominates in the U.S.; HIV-2 found in West Africa

HIV/AIDS

Epidemiology (continued)

Injection drug use (IDU) accounts for 43% of AIDS cases in women

Transmission is through sexual contact, parenteral exposure, and perinatal or postpartum contact

HIV/AIDS

Definition

Epidemiology

Clinical course

Treatment

HIV/AIDS

Clinical course

Primary HIV infection can be asymptomatic or result in an acute “viral” syndrome

Initial infection is followed by active viral replication primarily in lymphoid tissue

Course followed clinically with CD4 lymphocyte counts and viral RNA (viral load)

1. Active viral replication is at a rate of approximately 10 million viral particles daily.

HIV/AIDS

Clinical course (continued)

AIDS diagnosis is made using the 1993 CDC classification and case definition system

Progression from HIV positive to AIDS in 40-50% of patients within 7-10 years

1. The diagnosis of AIDS will be reviewed in more detail on the next slide.

HIV/AIDS

Clinical course (continued)

HIV-infected adults meet diagnostic criteria for AIDS if they have:

- a) a CD4 cell count of <200
- b) a CD4/total lymphocyte percentage of <14, or
- c) any one of the AIDS defining diagnoses included in the CDC's 1993 AIDS surveillance case definition

1. Examples of AIDS defining diagnoses in the CDC's 1993 definition include (but are not limited to):

- Candidiasis (of esophagus, bronchi, trachea, lungs)
- HIV-related encephalopathy
- Histoplasmosis (disseminated or extrapulmonary)
- Kaposi's sarcoma
- Burkitt's lymphoma
- Herpes simplex, chronic ulcer(s) (>1 month duration); or
bronchitis, pneumonitis, or esophagitis
- Mycobacterium avium* complex or *M. kansasii* (disseminated or
extrapulmonary)
- Mycobacterium tuberculosis* (any site)
- Pneumocystis carinii* pneumonia
- Recurrent pneumonia
- Progressive multifocal leukoencephalopathy
- Toxoplasmosis of the brain
- Wasting syndrome due to HIV

HIV/AIDS

Definition

Epidemiology

Clinical course

Treatment

HIV/AIDS

Treatment

Indications for initiation of antiretroviral therapy include:

- a) symptomatic HIV disease
- b) CD4 count <500 or viral load $>10,000$
- c) acute retroviral syndrome or within 6 months of documented seroconversion
- d) prevention of perinatal transmission
- e) post-exposure prophylaxis

HIV/AIDS

Treatment (continued)

Three classes of medications are effective in helping to decrease retroviral replication:

- a) reverse transcriptase inhibitors (e.g., Zidovudine)
- b) non-nucleoside reverse transcriptase inhibitors (e.g., Nevirapine)
- c) protease inhibitors (e.g., Indinavir)

1. Note that certain antiretroviral medications occupy the P450 3A4 system, and may thus interact with buprenorphine's metabolism. For example, Nevirapine induces P450 3A4 enzymes, so effects of buprenorphine could be diminished. On the other hand, ritonavir is an inhibitor of the P450 3A4 system. Since systematic studies of buprenorphine and various antiretroviral medications have not been conducted, the clinician should monitor the patient for signs and symptoms of opioid withdrawal or intoxication effects when new medications such as these are being started. It is also important to warn the patient about these possible medication interactions, so the patient is attentive to possible changes in efficacy of buprenorphine.

HIV/AIDS

Treatment (continued)

Current (2000) standard is at least a three-drug regimen and is frequently called highly active antiretroviral therapy (HAART)

HAART generally includes two reverse transcriptase inhibitors and at least one protease inhibitor

Monotherapy is no longer considered effective

HIV/AIDS

Treatment (continued)

Clinical trials have demonstrated non-detectable viral loads in 80% of patients receiving HAART

Patients with good adherence to HAART regimens have decreased morbidity, mortality, hospitalization rates, and viral replication

1.

HIV/AIDS

Treatment (continued)

Adherence to HAART can be difficult

Poor adherence to HAART predicts treatment failure and can lead to development of viral resistance

Side effects of HAART can include nausea, rash, and headache

Complications of HAART can include nephrolithiasis, anemia, pancreatitis, neuropathy, lipid abnormalities, and fat redistribution

1. Adherence to HAART can be difficult due to the complicated medication regimens.

HIV/AIDS

Treatment (continued)

Prophylaxis against opportunistic infections is indicated to decrease the incidence of *Pneumocystis carinii* pneumonia (PCP), toxoplasmosis, *Mycobacterium avium* complex (MAC) infection, tuberculosis, fungal infections (candidiasis, cryptococcosis), and cytomegalovirus (CMV).

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Tuberculosis

Epidemiology

Clinical presentation

Screening for tuberculosis infection

Interpretation of PPD results

Assessment of patients with a positive PPD

Treatment

Tuberculosis

Epidemiology

Worldwide, approximately 2 billion people (1/3 of world population) are infected with *M. tuberculosis*

Since the HIV pandemic began in the U.S. in the mid-1980s, there has been increased concern about TB since it is more common in this population

Tuberculosis is also more common in injection drug users in general and in patients with alcohol use disorders

1. There has been rising concern about tuberculosis since the mid-1980s, since TB is 200 times more common in persons who are HIV+ than those who are HIV-. In addition, strains of TB that are resistant to usual drug treatment regimens have been identified.

Tuberculosis

Epidemiology (continued)

Others at high risk for tuberculosis:

Ethnic minorities

Immigrants

Homeless persons

Nursing home residents

Patients with chronic disease or immune dysfunction

Tuberculosis

Epidemiology (continued)

Along with these patient groups, health care personnel including physicians, nurses, drug treatment program counselors, and others are at increased risk for tuberculosis infection

Tuberculosis

Epidemiology

Clinical presentation

Screening for tuberculosis infection

Interpretation of PPD results

Assessment of patients with a positive PPD

Treatment

Tuberculosis

Clinical presentation

Tuberculosis infection without disease: PPD+

Tuberculosis infection with disease: most commonly this involves pulmonary infection, although other sites can be involved as well. This is referred to as extra-pulmonary tuberculosis (and can involve sites such as bone, lymph node, kidneys, and other intra-abdominal organs)

1. Tuberculosis infection without disease is indicated by a positive PPD (purified protein derivative) test. PPDs will be reviewed in more detail later in the section.
2. Tuberculosis with pulmonary involvement typically involve the upper lobes. Symptoms can include cough, weight loss, night sweats, and hemoptysis.

Tuberculosis

Epidemiology

Clinical presentation

Screening for tuberculosis infection

Interpretation of PPD results

Assessment of patients with a positive PPD

Treatment

Tuberculosis

Screening for tuberculosis infection

Should be performed annually on all patients with a history of a substance abuse disorder who have previously been PPD– and have no prior history of tuberculosis

Patients who have had a previously positive PPD should not receive repeat PPD testing, but should be followed with annual chest x-rays

1. Tuberculosis screening is accomplished through administration of a PPD (along with control skin tests such as mumps, candida, etc.).

Tuberculosis

Epidemiology

Clinical presentation

Screening for tuberculosis infection

Interpretation of PPD results

Assessment of patients with a positive PPD

Treatment

Tuberculosis

Interpretation of PPD results

PPD read as positive if:

5 mm of induration: Patients with HIV infection, those with close contact to documented cases, and those who have chest x-rays suggestive of tuberculosis

Tuberculosis

Interpretation of PPD results (continued)

PPD read as positive if (continued):

10 mm of induration: Individuals from population groups with a high prevalence of tuberculosis infection including immigrants, injection drug users, homeless persons, immigrants from endemic areas

15 mm of induration: Individuals with no known risk factors for tuberculosis

Tuberculosis

Epidemiology

Clinical presentation

Screening for tuberculosis infection

Interpretation of PPD results

Assessment of patients with a positive PPD

Treatment

Tuberculosis

Assessment of patients with a positive PPD

History and physical exam focusing on risk factors for tuberculosis

Chest x-ray

Sputum studies (AFB smear and culture in individuals with chest x-ray evidence of possible tuberculosis)

Tuberculosis

Epidemiology

Clinical presentation

Screening for tuberculosis infection

Interpretation of PPD results

Assessment of patients with a positive PPD

Treatment

Tuberculosis

Treatment: No evidence of active disease (continued)

Criteria for which PPD+ patients should receive chemoprophylaxis have been developed by the CDC and other groups. Generally, patients under 35 years of age with a recent PPD conversion should be considered for INH chemoprophylaxis. However, all individuals who are HIV+, regardless of age, should be considered.

Tuberculosis

Treatment: No evidence of active disease

Isoniazid (INH) 300 mg po qd (plus daily vitamin B6) for six months is the standard therapy in immunocompetent patients

Isoniazid (INH) 300 mg po qd (plus daily vitamin B6) for one year is the standard therapy for HIV+ patients

1. Vitamin B6 is pyridoxine.

Tuberculosis

Treatment: No evidence of active disease (continued)

INH hepatotoxicity is a concern, especially in patients with other reasons to have liver disease. Thus, particularly in drug users, regular monitoring of liver enzymes (e.g., monthly) is important.

Tuberculosis

Treatment: Evidence of active disease

Most common presentation is pulmonary tuberculosis

Several different drug regimens available (each involves use of multiple medications)

Most common regimens include isoniazid (INH), rifampin, pyrazinamide, ethambutol, and other agents

1. Note that active tuberculosis must be reported to the local health authorities. Consultation with the local public health department or an infectious disease specialist should be considered when planning treatment of active TB.

Tuberculosis

Treatment: Evidence of active disease (continued)

Directly observed therapy may be particularly important when treating substance users who have active tuberculosis

Physicians need to be aware of the potential for drug resistant strains of *M. tuberculosis* in their patients and provide additional treatment as appropriate

1. Multidrug resistant strains of TB are likely to occur when patients are non-compliant with medications (and especially if they are non-compliant with one medication out of the multiple drug regimen prescribed). Resistant strains then become more difficult to treat. Compliance with taking all medications as prescribed is extremely important so as to lessen the risk of multidrug resistant strains developing.

Tuberculosis

Treatment: Adherence and directly observed therapy

Several approaches have been tested

Some groups have demonstrated that administering INH within substance abuse treatment programs can increase adherence with therapy

INH has been administered mixed with methadone

Creative approaches to increasing adherence with INH may protect patients and staff

1. In a study by O'Connor et al. (Addiction), INH was administered combined with methadone, for methadone maintained patients. 72% of patients completed their INH chemoprophylaxis. The most common reason for non-completion was discharge from methadone maintenance treatment.

[Reference:

O'Connor P.G., Shi J.M., Henry S., Durante A.J., Friedman L., Selwyn P.A. Tuberculosis chemoprophylaxis using a liquid isoniazid-methadone admixture for drug users in methadone maintenance. *Addiction* 94:1071-5, 1999.]

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Preventive Health Care

Specialized health care needs of opioid dependent patients

Infectious diseases

Other medical conditions

Routine screening activities

Routine vaccinations

Preventive Health Care

Specialized health care needs of opioid dependent patients

High prevalence of selected infectious diseases

May be at risk for other drug use-related complications,
such as hepatitis from alcohol use

Along with psychiatric conditions, also at risk for a
variety of social problems

Preventive Health Care

Specialized health care needs

Infectious diseases commonly seen in opioid dependent patients

Other medical conditions

Routine screening activities

Routine vaccinations

Preventive Health Care

Infectious diseases commonly seen in opioid dependent patients

Viral (Hepatitis A, B, C; HIV)

Tuberculosis (pulmonary, extrapulmonary)

Bacterial infections (soft tissue infections, pneumonia, endovascular infections (endocarditis))

Sexually transmitted diseases (e.g., syphilis, human papillomavirus)

1. Hepatitis A is transmitted via person-to-person contacts, by the fecal-oral route (e.g., contaminated water), or via contaminated shellfish or other foods. It is the most common cause of acute hepatitis in the United States.
2. Other sexually transmitted diseases include chlamydia, gonorrhea, and herpes simplex virus.
3. It is important to keep in mind these conditions in patients treated with buprenorphine, and to screen and treat them accordingly. One of the advantages to office-based treatment with buprenorphine is that integration of opioid dependence treatment with other medical services can occur. These other services include treatment of infections and STDs. The clinician should keep in mind these other medical disorders at all times, but especially early in the course of treatment of opioid dependence when patients are first stabilizing (and may suffer from abscesses, STDs, and other co-morbid conditions found among patients with opioid dependence).

Preventive Health Care

Specialized health care needs

Infectious diseases

Other medical conditions commonly seen in
patients with opioid dependence

Routine screening activities

Routine vaccinations

Preventive Health Care

Other medical conditions commonly seen in patients with opioid dependence

Alcoholic hepatitis

Cervical cancer

Respiratory tract cancers including lung, oropharynx, and larynx

1. Since it is likely patients will be seen in the office at least once per month, the clinician will have frequent opportunities to conduct screening for other health-related problems.

Preventive Health Care

Specialized health care needs

Infectious diseases

Other medical conditions

Routine screening activities for patients with opioid dependence

Routine vaccinations

Preventive Health Care

Routine screening activities for patients with opioid dependence

Viral: Hepatitis B, C: Screening antibody tests and liver enzymes

Tuberculosis: Annual screening with PPD and/or chest x-ray

Syphilis: Annual VDRL or RPR (and FTA if indicated)

Preventive Health Care

Routine screening activities for patients with opioid dependence (continued)

HIV infection: HIV antibody testing to be offered initially and repeatedly as indicated; those who are HIV+ are typically followed with CD4 cell counts and viral load studies

Cervical cancer: Yearly screening, more frequent (q6month) in those with prior abnormalities or very high risk

1. Patients who test positive for HIV should be provided counseling regarding HIV infection. If more extensive counseling is needed and is not available through the office, then appropriate referral for the HIV+ patient should be made. If the patient tests negative but is still at risk for HIV infection, then counseling (e.g., regarding high risk behaviors and transmission) should be provided.

Preventive Health Care

Specialized health care needs

Infectious diseases

Other medical conditions

Routine screening activities

**Routine vaccinations to be considered in patients
with opioid dependence**

Preventive Health Care

Routine vaccinations to be considered in patients with opioid dependence

Pneumococcal vaccine

Influenza vaccine

Haemophilus influenza vaccine

Hepatitis A

Hepatitis B

Tetanus

Outline for This Talk

- I. Hepatitis B
- II. Hepatitis C
- III. HIV/AIDS
- IV. Tuberculosis
- V. Preventive health care for opioid dependent patients
- VI. Summary

Summary

Patients with opioid dependence frequently have co-morbid medical conditions, especially infectious diseases

Important to screen for these disorders, and to provide treatment and prevention interventions (or to be aware of and familiar with screening, treatment, and prevention services if done elsewhere)

Linkage of substance abuse treatment with medical treatments and prevention for co-morbid disorders can enhance medical treatment outcomes

Special Treatment Populations

Special Treatment Populations

The purpose of this talk is to review the use of buprenorphine in special populations of patients. However, there are few controlled studies conducted with these special treatment groups and buprenorphine. (Indeed, there are few controlled studies with these groups and methadone, as well.)

The use of buprenorphine in special populations is an important topic, as it is not infrequent to see opioid dependent patients with characteristics that can be considered atypical. Some of these patients – such as adolescents with opioid dependence – may specifically seek out office-based buprenorphine treatment rather than other medications such as methadone treatment. Thus, the importance of being familiar with the characteristics of special populations and the use of buprenorphine in these circumstances.

Outline for This Talk

- I. Adolescents
- II. Pregnant patients
- III. Geriatric patients
- IV. HIV positive patients
- V. Acute and chronic pain patients
- VI. Patients with renal failure
- VII. Summary

1. We will review special treatment considerations, especially as they relate to buprenorphine use, in the following populations of patients who have been diagnosed with opioid dependence.

Outline for This Talk

- I. Adolescents
- II. Pregnant patients
- III. Geriatric patients
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1. We'll begin by talking about adolescents. We should note that there is no specific age range that defines "adolescence." In some ways, we probably all have known 16 year olds who seem wise beyond their years, and people in their 30s (and older) who are "stuck in adolescence." For our purposes, we're going to focus on issues associated with the treatment of patients who are <18 years of age.

Adolescents

Prevalence of heroin use

Special diagnostic and treatment considerations

Use of buprenorphine with adolescents

1. We'll begin this section by reviewing data on the prevalence of heroin use in adolescents.
2. This is limited to heroin use, rather than the broader category of illicit opioid use, because the data set available is restricted to heroin use only.

Prevalence of heroin use

In 1998, for 12-17 year olds:

Ever used: 80,000

Used in past year: 58,000

In 1998, for 18-25 year olds:

Ever used: 303,000

Used in past year: 111,000

1. These rates are from the National Household Survey on Drug Abuse: Population Estimates 1998 (www.samhsa.gov/oas).
2. Note that experimentation does not inevitably lead to dependence. These figures do not reflect numbers who are dependent.
3. Data for 18-25 year olds is provided for contrasting.
4. From the same report, information is available about needle use for these age groups. (Note, however, that this is needle use for any drug – it is not limited to just heroin. While it is probable most needle use is heroin use, it also may be the case that a substantial number of persons are injecting cocaine rather than heroin.)

Needle use

12-17 year olds:

Ever used needles: 75,000

Used needles in past year: 27,000

18-25 year olds:

Ever used needles: 300,000

Used needles in past year: 121,000

5. Preliminary results from the 1999 NHSDA are available and they show there were an estimated 417,000 new users of heroin between 1996 and 1998, with 125,000 of these new users <18 years old, and 222,000 between 18-25 years old (at the time of first use). Most of these new users had not injected heroin (only 37% reported they had ever injected heroin).

Adolescents

Prevalence of heroin use

Special diagnostic and treatment considerations

Use of buprenorphine with adolescents

1. Next, we're going to briefly review some special considerations associated with diagnosing and treating adolescent, opioid dependent patients.

Special diagnostic and treatment considerations

Length of time illicit opioids used

Relatively short?

Route of administration

Injecting?

At risk for HIV or other infections?

Several questions should be asked when initiating treatment of adolescents.

1. What is the length of time they have been using illicit opioids? Is this a new problem, or one which has been in place for many months or even years? (Buprenorphine may be the first choice for young patients who are early in their history of opioid dependence. There may be advantages – both pharmacologic and sociologic – to not exposing younger patients to the methadone treatment system – a system that may expose them to a broader segment of the drug-using culture.)
2. What is the route of administration? Is the patient injecting opioids? Is he/she at risk for HIV or other infections? (The risk for infectious illnesses and overdose deaths suggests that treatment should be aggressive for such young patients, especially if they have progressed to injecting drug use.)

These considerations continue on the next slides.

Special diagnostic and treatment considerations

Use versus abuse versus dependence

Severity of use?

Evidence of physical dependence?

Goals of treatment intervention

Withdrawal off opioids?

Maintenance?

3. What is the severity of use? Is this experimentation that has occurred sporadically? Sporadic use needs to be addressed and treated, starting with non-pharmacologic approaches. It is highly unlikely it needs to be treated with a medication such as buprenorphine. Is there evidence the patient has become physically dependent on opioids? If so, it suggests that pharmacological treatment will be needed. Is there evidence (or strong indication) that the patient's use will quickly become dependence in spite of other treatment approaches? If so, it suggests that treatment with buprenorphine should be considered.

4. What is the goal of the treatment intervention? Withdrawal off opioids? Maintenance on opioids? (The latter may be reserved for adolescent patients who have failed previous attempts at withdrawal. In addition, adolescent patients who are not currently dependent but have been in the past and have a history of multiple relapses should be considered for maintenance even if their current relapse has not yet progressed to dependence.)

Special diagnostic and treatment considerations

Consent for treatment

Need to include parents?

(Will vary from state to state.)

5. Can the adolescent (person <18 years old) provide consent for treatment without inclusion of a parent? This is a complicated topic that can vary on a state by state basis. It is important to know local laws governing treatment. In some states, adolescents can enter treatment without parental consent, while in other states parental consent must be obtained. (However, further complicating matters is the status of the adolescent; is he/she an emancipated minor – that is, a parent, married, in the armed services, etc.? Emancipated minors are legally considered an adult even though their age is less than 18 years). State law on parental consent is also important to know when considering talking with parents about the adolescent's treatment – consent may be needed from the adolescent in order to talk with the parents.

It is also important to determine who is the parent? (Biological parent, foster parent, the state?) Even if the adolescent can consent for treatment, should the parent be included in the discussion of the treatment plan? (Treatment planning decisions should include the adolescent initially.)

Adolescents

Prevalence of heroin use

Special diagnostic and treatment considerations

Use of buprenorphine with adolescents

1. Finally, we will briefly discuss the use of buprenorphine in adolescent patients.

Use of Buprenorphine with Adolescents

While extensive use of buprenorphine in adults, limited use in adolescents

Guidelines for dose induction and withdrawal recommended for adults should, in general, be used with adolescents

Assess level of physical dependence, adjust dose accordingly for adolescents, just as for adults

1. There have been no controlled studies of buprenorphine dosing in adolescents.
2. In general, guidelines for adults should be used when treating adolescents.
3. Use buprenorphine alone for induction, then the buprenorphine/naloxone combination for maintenance and withdrawal.

Use of Buprenorphine with Adolescents

Buprenorphine may be a good match for patients with lower levels of physical dependence (such as adolescents)

A history of multiple relapses (e.g., after medically supervised opioid withdrawals) is an indicator for a trial of buprenorphine maintenance treatment

Buprenorphine's possible mild withdrawal syndrome may also make it particularly useful in adolescents

1. Recall that buprenorphine itself produces a low level of physical dependence. Thus, it may be particularly well suited for patients with low levels of physical dependence (such as those early in their dependence history, like adolescents).
2. For adolescents who relapse after undergoing repeated episodes of medically supervised opioid withdrawal (e.g., inpatient detoxifications), a trial of office-based buprenorphine maintenance may be indicated.
3. Buprenorphine may have a milder withdrawal syndrome than full agonist opioids like methadone. (This has been frequently hypothesized, although not tested by well-controlled studies.) If buprenorphine does have a milder withdrawal syndrome, this may also be an advantage over methadone for its use in this population (especially if the goal is eventual withdrawal off the medication).

Use of Buprenorphine with Adolescents

Supervision of take home doses of medication

Watch for risk of diversion, abuse

Assess for pregnancy

Provide other levels of treatment beyond medication

Use the same considerations which apply to adults – should the patient be in charge of medication, or some other responsible family member (such as a non-substance using parent)? Is there a chance that the female patient is pregnant, and what are the non-pharmacological services that will be provided? The age of the patient should not lead to any assumptions or any compromise in the treatment approach (e.g., assuming that the young female cannot be pregnant, that the young opioid dependent patient will not need other non-pharmacological services).

Considerations for use of buprenorphine in adolescents:

1. What is their expected level of adherence to the treatment plan? The treatment plan should address who should be in charge of take-home doses of the medication (i.e., patient versus parent). Is there a risk the adolescent will divert or abuse take home doses?
2. The decision of how many days of medicine should be given to an adolescent for use at home is made on the same criteria as for an adult, taking into consideration factors such as the stability of the home environment and the level of involvement of parents in the adolescent patient's treatment.
3. Is there a chance the female adolescent is pregnant? If she is, then consider maintenance rather than buprenorphine withdrawal. Or, consider referral to methadone treatment if indicated (e.g., need for daily supervision of treatment progress, patient willingness, availability of specialized on-site obstetric care).
4. What other services will be provided to the patient? Don't simply rely on buprenorphine alone – consider non-pharmacological services (either office based or elsewhere), such as specialized groups for adolescent substance abusers.

Outline for This Talk

- I. Adolescents
- II. Pregnant patients**
- III. Geriatric patients
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- VI. Patients with renal failure
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1. Next we'll turn to a discussion of the management of the pregnant, opioid dependent woman.

Pregnancy

Initial management of the pregnant patient

Evaluation of the patient

Use of buprenorphine versus methadone

In utero exposure to buprenorphine

Buprenorphine dosing during postpartum

1. Before getting into the use of buprenorphine in pregnant, opioid dependent women, we'll first review some more general issues associated with this patient population.
2. Let's begin with some points about the initial management of the pregnant, opioid dependent patient.

Initial Management of the Pregnant Patient

It is important to know about specialized treatment services available for pregnant, opioid dependent patients in your community. Management of the patient will depend on the availability of such services.

1. It is important to know about specialized treatment programs in the local geographical area for pregnant women who abuse substances.

Initial Management of the Pregnant Patient

If specialized treatment program is available:

and it is a new patient – refer to the program

and it is a buprenorphine/naloxone maintained patient
who is now pregnant:

switch to buprenorphine

consider referral to the program

1. If a specialized treatment program for opioid dependent pregnant women is available, and you are seeing a new patient who qualifies for that program (i.e., she is pregnant and opioid dependent), then refer her to that program (immediately).
2. If you have a patient you have been following for some time who is maintained on buprenorphine/naloxone and becomes pregnant, then
 - a.) switch her to buprenorphine only (i.e., buprenorphine monotherapy) to minimize risk of naloxone exposure. While teratogenic effects of naloxone are not known, exposure of the fetus to naloxone should be minimized to avoid risk not known at present
 - b.) give strong consideration to referring the patient to the specialized treatment program; if the program does not provide integrated prenatal care, then refer to a prenatal care provider as well
 - c.) refer the patient to prenatal care provider immediately if there is any delay in access to the specialized treatment program, or if no such program is available

Pregnancy

Initial management of the pregnant patient

Evaluation of the patient

Use of buprenorphine versus methadone

In utero exposure to buprenorphine

Buprenorphine dosing during postpartum

Evaluation of the Pregnant Patient

Factors to consider in the evaluation:

Is the patient dependent on opioids?

Is there other drug use?

Medical problems?

Psychiatric problems?

Family and social situation?

1. When evaluating the pregnant, opioid dependent woman, consider the sorts of questions shown in the slide.
2. If the patient is not dependent on opioids but is abusing opioids, then is it possible to achieve cessation of opioid use (and the risks associated with such use) – perhaps through non-pharmacological interventions such as treatment at an intensive level of treatment (e.g., inpatient, partial hospitalization program)? On the other hand, if the patient is dependent upon opioids, then stabilization on medication should be the goal.
3. Other drug use (in addition to opioid use) suggests treatment interventions will need to be more extensive, and the patient may be better served in a more comprehensive substance abuse treatment program rather than office-based treatment.
4. Similarly, medical and/or psychiatric problems suggest that more intensive services may be needed to promptly address and stabilize the pregnant patient.
5. Finally, the family and social situation of the patient can guide the decision about whether to provide office-based buprenorphine treatment or refer the patient. Strong, stable family and social supports suggest office-based treatment can be successful for the pregnant patient. Unstable family and social supports (e.g., substance using family members, homelessness) suggest the patient will require intensive and comprehensive treatment and social services, which may be better delivered via a specialized program for substance abusing patients.

Evaluation of the Pregnant Patient

Determine if patient has regular prenatal care provider, and if prenatal care has been initiated

Obtain consent to communicate with prenatal care provider

Provide nutritional counseling specific to pregnancy, if indicated (e.g., use of prenatal vitamins and iron)

1. During the initial evaluation of the pregnant patient, determine if the patient has a regular prenatal care provider. Obtain consent to talk to the provider, if she has one. Be prepared to answer questions the provider may have about buprenorphine treatment for opioid dependence.
2. If the patient does not have a prenatal care provider, make the referral immediately. In addition, provide the patient with nutritional counseling specific to the use of prenatal vitamins and iron (if such has not been obtained by the patient already).

Pregnancy

Initial management of the pregnant patient

Evaluation of the patient

Use of buprenorphine versus methadone

In utero exposure to buprenorphine

Buprenorphine dosing during postpartum

[References:

Fischer, G., Johnson, R.E., Eder, H., Yagsch, R., Peternell, A., Wehinger, M., Langer, M., Aschauer H.N. Treatment of opioid-dependent pregnant women with buprenorphine. *Addiction* 95:239-244, 2000.

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Marquet, P., Lavignasse, P., Chevrel, J., Lach,tre, G., Merle, L. 1998. In utero exposure to subutex induces no or mild withdrawal syndromes in the newborn. *Thérapie*. 53, p 178.]

Use of Buprenorphine versus Methadone

Methadone approved for use in pregnancy, and substantial experience with it

Not a similar amount of experience with buprenorphine use in pregnancy

1. Methadone is approved for use during pregnancy, and there is substantial experience with it. The pregnant woman's methadone dose may need to be increased during pregnancy, or split dosing instituted (due to increased metabolism). The neonate of a mother maintained on methadone will withdraw off methadone, and may need pharmacological management in the nursery.
2. While methadone maintenance has been extensively used with pregnant women, there is much more limited work and experience with buprenorphine maintenance during pregnancy. However, there has been interest in buprenorphine use during pregnancy, because it has been hypothesized that the neonatal withdrawal syndrome should be milder than that seen with methadone.

[Reference:

Fischer, G., Jagsch, R., Eder, H., Gombas, W., Ethzersdorfer, P., Schmidl-Mohl, K., Schatten, C., Weinger, M., Aschauer, H.N. 1999. Comparison of methadone and slow-release morphine maintenance in pregnant addicts. *Addictions*. 94 (2), 231-239.

Harper, R.G., Solish G., Feingold E., Gersten-Woolf N.B., Sokal, M.M. 1977. Maternal ingested methadone, body fluid methadone, and the neonatal withdrawal syndrome. *Am. J. Obstet. Gynecol.* 129, 417-424.

Jarvis, M.A.E. and Schnoll S.H. 1994. Methadone treatment during pregnancy. *J. Psychoactive Drugs*, 26(2), 155-161.]

Use of Buprenorphine versus Methadone

Minimal information about need for dose adjustments of buprenorphine during pregnancy

Pregnant women treated with buprenorphine have had good withdrawal suppression with once daily dosing

Maintain clinical flexibility during pregnancy – consider dose adjustments if indicated

1. Pregnant women have been maintained on up to 12 mg/day of buprenorphine tablets. (This is approximately equivalent to 6-8 mg per day of buprenorphine solution.)
2. There have not been reports suggesting altered metabolism of buprenorphine during pregnancy (as there can be with methadone). Thus, there is no evidence of a need to use split-dosing of buprenorphine.
3. However, the physician should maintain clinical flexibility when using buprenorphine during pregnancy. If the patient reports her dose no longer provides adequate effects for a 24 hour period (such as blockade or withdrawal suppression), then dose increases or more frequent dosing should be given. If clinically indicated, dose adjustments should be made during pregnancy.

Use of Buprenorphine versus Methadone

Buprenorphine may have milder withdrawal syndrome for infant

Low levels of buprenorphine in breast milk (and poor oral bioavailability when swallowed)

Probably should not use buprenorphine/naloxone

1. As noted earlier, buprenorphine may have a milder withdrawal syndrome for the infant (relative to methadone).
2. Studies of buprenorphine in breast milk have shown low levels of buprenorphine. Since buprenorphine has poor oral bioavailability, and the infant will swallow the breast milk, it is likely no systemic buprenorphine will be delivered if the mother breast feeds. Thus, breast feeding can be recommended to the buprenorphine maintained mother.
3. It is probably best to not use buprenorphine/naloxone during pregnancy. There is no benefit in fetal exposure to naloxone. While there is no known risk, there is very little information about the consequences to the fetus of chronic naloxone exposure in utero (so risk is unknown, rather than known). Given this unknown risk, no benefit ratio, it is best to switch the pregnant woman to buprenorphine alone if she is on buprenorphine/naloxone and becomes pregnant.

Pregnancy

Initial management of the pregnant patient

Evaluation of the patient

Use of buprenorphine versus methadone

In utero exposure to buprenorphine

Buprenorphine dosing during postpartum

In Utero Exposure to Buprenorphine

Limited experience with buprenorphine in pregnancy
(primarily case reports and small series of patients)

No significant adverse effects on fetus noted

Neonate is dependent on opioids if mom maintained on
buprenorphine

However, neonatal abstinence syndrome (NAS) minimal and
short lived in buprenorphine-exposed infants

1. In general, births for buprenorphine maintained women have been full-term, with weights in the normal range. No significant problems have been noted.

Pregnancy

Initial management of the pregnant patient

Evaluation of the patient

Use of buprenorphine versus methadone

In utero exposure to buprenorphine

Buprenorphine dosing during postpartum

Buprenorphine Dosing During Postpartum

Continue mother on buprenorphine (even if she is breast feeding)

Consider dose adjustments if indicated

1. After delivery, the patient should be monitored for dose adjustments. For example, if the patient has received split dosing during pregnancy, then resumption of daily dosing could occur.

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- VI. Patients with renal failure
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1. The next special population group is opioid dependent geriatric patients.
2. There is no generally accepted definition of elderly. For purpose of this discussion, we will refer to patients who are over 60 years of age.

[Reference:

Blow F.C. Substance Abuse Among Older Adults. Treatment Improvement Protocol (TIP0 #26, U.S. Department of Health and Human Services, Center for Substance Abuse Treatment, Rockville, Maryland, 1998.]

Geriatric patients

Prevalence of illicit opioid use

Special diagnostic considerations

Special treatment considerations

Use of buprenorphine with geriatric patients

Prevalence of Illicit Opioid Use

No information available

National Household Survey classifies as 35+ years old

Drug Abuse Warning Network classifies as 55+ years old

Anecdotal reports of older patients in methadone treatment

1. There is no good epidemiological information about the prevalence of illicit opioid use in the elderly. The surveys sponsored by the federal government classify people into age groups that mix the middle-aged and the elderly.
2. Methadone treatment programs report treating patients who are older (e.g., over 60 years). However, it is not known how many of these patients enter treatment later in life, versus those who have been in treatment for many years.
3. While there is essentially no good information about rates of illicit opioid use in the elderly, it is worth noting that alcohol abuse and dependence occurs in this age group. Thus, dependence on psychoactive substances can certainly be present in the later years of life.

Geriatric patients

Prevalence of illicit opioid use

Special diagnostic considerations

Special treatment considerations

Use of buprenorphine with geriatric patients

Special Diagnostic Considerations

The usual diagnostic criteria may be less appropriate for the elderly

Effects of drug use may be mistakenly attributed to aging

Don't usually think of drug use in the elderly

1. It may be easier to miss the diagnosis of opioid dependence in the elderly.
2. For example, some criteria may be less relevant (such as those related to violations of social norms).
3. Effects of drug use (such as lapses in memory, lethargy) may be attributed to aging, rather than recognized as symptomatic of illicit substance use.
4. We don't readily think of drug use – especially opioid use – as a problem in the elderly; our index of suspicion may be too low.

Geriatrics

Prevalence of illicit opioid use

Special diagnostic considerations

Special treatment considerations

Use of buprenorphine with geriatric patients

Special Treatment Considerations

Co-morbid medical problems

Other medications

1. Pharmacologic management of elderly, opioid dependent patients may be complicated by their co-morbid medical conditions, as well as their need to be taking other medications. For example, co-morbid medical conditions may make frequent office visits difficult when the patient is starting on buprenorphine. Compromised respiratory status may necessitate closer monitoring while being maintained on a potential respiratory depressant. Ready access to needles in the diabetic opioid user may lead to concerns about injecting drug use by the patient, or diversion of needles and subsequent non-compliance in taking insulin.

Geriatric patients

Prevalence of illicit opioid use

Special diagnostic considerations

Special treatment considerations

Use of buprenorphine with geriatric patients

Use of buprenorphine with geriatric patients

No data on buprenorphine for opioid dependence in the elderly

Consider more gradual dose induction and closer monitoring (versus routine practice in non-elderly)

Watch for medication interactions

1. At the onset of treatment with buprenorphine, more frequent monitoring of the patient should occur. This monitoring should assess the patient for medication side effects, including increased sensitivity to lower doses of buprenorphine.
2. A review of medication interactions is covered in the pharmacology lecture.

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- I. Adolescents
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- IV. HIV-positive patients**
- V. Acute and chronic pain patients
- VI. Patients with renal failure
- VII. Summary

[References:

Montoya I.D., Umbricht A., Preston K.L. Buprenorphine for human immunovirus-positive opiate-dependent patients. *Biol Psychiatry* 38:131-6, 1995.

Moatti J.P., Carrieri M.P., Spire B., Gastaut J.A., Cassuto J.P., Moreau J. Adherence to HAART in French HIV-infected injecting drug users: the contribution of buprenorphine drug maintenance treatment. *AIDS* 14:151-155, 2000.]

HIV-Positive Patients

Reports of buprenorphine use in HIV-positive patients

No adverse consequences associated with use of buprenorphine in this population

Be aware of buprenorphine and antiretroviral medication interactions (protease inhibitors metabolized by P450 3A4 – would increase buprenorphine levels)

1. Buprenorphine has been used extensively in HIV-positive patients – in particular, in France (where buprenorphine is the primary opioid maintenance medication).
2. There have been no reports of adverse consequences with use of buprenorphine in HIV-positive patients.
3. Be aware of buprenorphine's possible interaction with antiretroviral medications. For example, there is some evidence to suggest ritonavir and indinavir may alter buprenorphine metabolism. This seems to be less the case with saquinavir, another protease inhibitor.

HIV-Positive Patients

Consider referral to specialized treatment programs for HIV-positive patients (if available)

Outcomes may be better when enhanced services provided

1. Thus, know if specialized HIV services are available in the area, and consider referral to such.
2. It may be best to provide buprenorphine along with specialized, enhanced treatment services for HIV-positive patients.

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Acute and Chronic Pain Patients

General points regarding pain treatment

Treatment of acute pain in patients maintained on buprenorphine

Treatment of chronic pain in patients with opioid dependence

General Points Regarding Pain Treatment

Buprenorphine is an effective parenteral analgesic, but duration of analgesia is relatively short (necessitating multiple dosing daily)

In United States, sublingual form has not been developed for analgesic purposes

Use of full opioid agonists to treat pain in patients maintained on buprenorphine can be complicated

1. It is probable that the sublingual form of buprenorphine could be used for the treatment of pain. However, in the United States this formulation has not been developed for such an indication. (In other countries, a sublingual form of buprenorphine is available for use in the treatment of pain.) In the United States, only the injectable form of buprenorphine is approved for the treatment of pain.
2. If sublingual buprenorphine were used for the treatment of pain, then the dosing frequency would need to be increased. Buprenorphine's analgesic duration is only a few hours.
3. The treatment of pain in patients maintained on buprenorphine can be complicated, as will be discussed further in the next slides.

NOTE: Additional information on the treatment of patients who suffer from chronic pain can be found in the Appendix to this section.

Acute and Chronic Pain Patients

General points regarding pain treatment

Treatment of acute pain in patients maintained on buprenorphine

Treatment of chronic pain in patients with opioid dependence

Acute Pain in Buprenorphine Maintained Patients

Make sure some form of opioid maintenance medication is continued (buprenorphine, methadone, LAAM)

If maintaining patient on buprenorphine, initially try non-opioid analgesics

If opioid analgesics required, consider switching off buprenorphine (e.g., to methadone)

Acute pain is not addressed by the maintenance dose of the opioid

1. For the buprenorphine-maintained patient experiencing acute pain, management of the pain should first be attempted with non-opioid analgesics.
2. If these are not sufficiently effective, then opioid analgesics can be used; however, it is important to keep in mind the potential for buprenorphine to precipitate withdrawal in a person receiving full agonist opioids (such as morphine). Thus, it may be prudent to switch the patient from buprenorphine maintenance to an alternate maintenance medication, such as methadone.
3. The patient's acute pain will not be treated by their once daily maintenance dose of buprenorphine. Other management of pain will be required.

Acute and Chronic Pain Patients

General points regarding pain treatment

Treatment of acute pain in patients maintained on buprenorphine

Treatment of chronic pain in patients with opioid dependence

Chronic Pain Patients

If patient will require opioids for treatment of chronic pain, then may be better to use methadone or LAAM as the treatment for opioid dependence

Avoids complications of possible precipitated withdrawal by buprenorphine

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[Reference:

Hand C.W., Sear J.W., Uppington J., Ball M.J., McQuay H.J., Moore R.A.
Buprenorphine disposition in patients with renal impairment: single and
continuous dosing, with special reference to metabolites. Br J Anaesth 64:276-
82, 1990.]

Patients with Renal Failure

Few studies, primarily single dose or short duration (for analgesia)

No significant difference in kinetics of buprenorphine in patients with renal failure versus healthy controls

No significant side effects in patients with renal failure

1. There is limited information about the use of buprenorphine in patients with renal failure – primarily pharmacokinetic studies in patients following operative procedures. The doses used in these studies were analgesic doses, which are lower than doses used in the treatment of opioid dependence (i.e., doses tested were 0.3 mg IV).
2. Results suggest it should be okay to use buprenorphine in patients with renal failure – consistent with buprenorphine's metabolism being hepatic (not renal).

Outline for This Talk

- I. Adolescents
- II. Pregnant patients
- III. Geriatric patients
- IV. HIV positive patients
- V. Acute and chronic pain patients
- VI. Patients with renal failure
- VII. Summary

Summary

Limited information about the use of buprenorphine for the treatment of opioid dependence in special populations of patients

This reflects, in part, the lack of studies with these groups (for any treatment intervention)

While caution should be exercised in the use of buprenorphine with any of these groups, buprenorphine's safety profile is an advantage to its use in these populations

Appendix to
Special Treatment Populations:
Chronic Pain

Physicians who treat opioid dependent patients with buprenorphine may find that patients with chronic pain seek out their assistance as well. While the sublingual form of buprenorphine is not approved for the treatment of chronic pain in the United States, it is awaiting final approval by the Food and Drug Administration (FDA) for the treatment of opioid dependence.

1. This appendix focuses upon patients who have chronic pain but who are not addicted to opioids (i.e., do not have a syndrome of dependence, as described in the Patient Assessment section).
2. The injectable form of buprenorphine (Buprenex) is marketed in the United States for the treatment of moderate to severe pain.

The purpose of this section is to provide a brief review of chronic pain, to aid the physician in understanding the clinical features and basic principles of management of chronic pain patients. If the clinician chooses to use sublingual buprenorphine to treat patients with chronic pain, then familiarity with the features of chronic pain and its treatment are important to know.

1. Note that use of sublingual buprenorphine for the treatment of chronic pain would be “off-label” use of this medication. Furthermore, patients treated with sublingual buprenorphine for chronic pain should not be counted toward the statutory limit of 30 patients that can be treated for opioid dependence (under the Federal waiver).

Chronic Pain and Opioids

Prevalence and assessment

Chronic pain is prevalent

Techniques for the precise diagnosis of many chronic pain syndromes are lacking

85% of patients with chronic low back pain cannot receive a precise diagnosis

1. The general point prevalence of chronic pain (due to any cause) is 17%.
2. While chronic pain is a common disorder, techniques for the diagnosis of many chronic pain syndromes are lacking.

[Reference:

Gureje O., Von Korff M., Simon G.E., Gater R. Persistent pain and well-being: a World Health Organization study in primary care. JAMA 280:147-51, 1998.]

Chronic Pain and Opioids

Prevalence and assessment (continued)

Patients with chronic pain do not display typical signs and symptoms of acute pain

Use validated scale to assess pain and accept patient self-reports

1. An example of a scale that can be used to assess pain is a visual analog scale ranging from 0 to 10, with 10 being the worst pain imaginable.
2. It is important to recognize and accept the patient's self-reports of his/her pain.

Chronic Pain Patients

Treatment

Exercise is beneficial for many chronic pain syndromes

For many other standard treatments, the effectiveness is low or not well documented

Case series studies suggest that opioids are safe and effective for many patients

1. The treatment for chronic pain can include a variety of interventions (both pharmacological and non-pharmacological). The use of opioids for the treatment of chronic pain is primarily based upon case series studies rather than large, double-blind and randomized clinical trials. These case studies do suggest that opioids can be safe and effective in the treatment of chronic pain.

Chronic Pain Patients

Treatment (continued)

Long-term randomized controlled trials have not been performed

Trials of opioid treatment are indicated for patients who have moderate to severe pain, significant functional interference, and poor response to other treatments

Chronic Pain Patients

Drug dependence and use of opioids for chronic pain

Drug dependence (addiction):

Continued substance use despite repeated negative consequences of drug use

Difficulty controlling use

1. The use of opioids for the treatment of chronic pain has been controversial. In part, this is due to concerns that patients without a history of abusing opioids may become addicted (i.e., develop a syndrome of dependence) to their prescription opioids and experience characteristics such as continued use despite repeated negative consequences, difficulty controlling use, etc. (although it is generally accepted that this concern is not substantiated by clinical experience).
2. In order to understand the appropriate medical use of opioids for the treatment of chronic pain, it is important to recognize the differences between drug dependence (addiction) and the use of prescriptive opioids for chronic pain treatment.
3. Drug dependence (addiction) is characterized by a variety of features, including continued use despite negative consequences, and difficulty controlling use of the substance. Other features can include intrusive thoughts about using the substance, a compulsive (or driven) pattern of use, and physical dependence on the substance. (These aren't the only features of drug dependence (addiction), and more information about the diagnosis of drug dependence is in the section on Patient Assessment/Selection.) Behaviors associated with drug dependence (addiction) include "doctor shopping" (seeking out different physicians for multiple prescriptions of abusable medications), and use of multiple pharmacies (to decrease suspicion when filling multiple prescriptions of abusable medications).

Chronic Pain Patients

Drug dependence and use of opioids for chronic pain (continued)

Of patients who take opioids for chronic pain:

Many become physically dependent

Most improve function and enjoy positive
consequences

Most remain in control of their opioid use

Few become addicted

1. In contrast to patients who are addicted, among patients who take opioids for chronic pain the pattern of use is different. While these patients may become physically dependent on opioids, most improve in psychosocial functioning, control their opioid use, and do not show the features of dependence reviewed in the previous slide.

Chronic Pain Patients

Drug dependence and use of opioids for chronic pain (continued)

Physical dependence:

Not a clinical problem as long as patients do not suddenly stop or decrease their opioids

Opioid withdrawal is uncomfortable but not life threatening for otherwise healthy individuals

1. It is worth noting that physical dependence on opioids is not considered a problem for pain patients. Patient who abuse opioids and those being appropriately treated with opioids for chronic pain can become physically dependent on opioids. However, this becomes problematic only if the patient suddenly stops (or substantially decreases) the opioids invoking the withdrawal syndrome. Opioid withdrawal – while very uncomfortable – is not life-threatening to otherwise healthy individuals.

Chronic Pain Patients

Drug dependence and use of opioids for chronic pain (continued)

A syndrome of dependence (“addiction”) characterized by:

- Continued use despite negative consequences
- Difficulty controlling use
- Compulsion to use

1. In contrast to physical dependence, the syndrome of dependence as defined by DSM-IV (or “addiction”) involves a broader array of symptoms such as continued use despite negative consequences, difficulty controlling use, and a compulsive pattern of use. These features of the syndrome of dependence highlight how the pattern to drug use has become problematic for the user.

Chronic Pain Patients

Addiction versus physical dependence

Syndrome of dependence – Patient focused on obtaining substances for:

Euphoria

Satisfying craving

Feeling normal

Avoiding withdrawal

Chronic Pain Patients

Syndrome of dependence versus physical dependence (continued)

Physical dependence:

Focus on obtaining opioids for pain relief

Undertreatment of pain can lead to manipulation,
doctor shopping, multiple ED visits

Pain patients (especially those with undertreated
pain) can be mistakenly labeled as drug
abusers/addicts

1. In contrast to patients who have a syndrome of dependence on a substance, physically dependent patients focus upon obtaining opioids for pain relief. While they may engage in behaviors that are similar to those seen in addicted patients (e.g., doctor shopping, multiple emergency department visits), these behaviors tend to remit once adequate treatment of their pain has been achieved.
2. Some clinicians have proposed a distinction between the syndrome of dependence (“addiction”) and “pseudoaddiction.” Addicted patients use substances because they produce euphoria, satisfy craving, provide a feeling of being normal, and help to avoid withdrawal; this pattern of addiction includes continued use despite negative consequences, difficulty controlling use, etc. Pseudoaddiction is a pattern of use and behavior that is similar to addiction, but that remits once adequate treatment of pain has occurred. The term pseudoaddiction is not a commonly used diagnostic category (it is not a DSM-IV diagnosis, for example), but it may aid in understanding that behavior of some patients can be related to a chronic pain disorder rather than addiction.

Chronic Pain Patients

Pain syndromes treated with opioids

- Cancer pain
- Chronic back pain
- Arthritis/rheumatologic conditions
- Neuropathy
- Phantom limb pain
- Post-herpetic neuralgia
- Fibromyalgia

1. A variety of pain conditions may be treated with chronic use of opioids.

Chronic Pain Patients

Pain syndromes not treated with opioids

Tension headache

Migraine headache

1. However, chronic use of opioids for the treatment of tension and migraine headaches is generally not indicated.

Chronic Pain Patients

Factors which make chronic pain patients more challenging

History of drug diversion

History of substance abuse disorders

Active suicidality

Personality disorders

Hepatic or renal disease

1. When managing patients with chronic pain, it is useful to recognize characteristics that are associated with increased difficulty in managing the patient. These factors can include a history of drug diversion or a substance abuse disorder, active suicidal ideation, personality disorders, and hepatic or renal disease.

Chronic Pain Patients

Goals of treatment

- Pain reduction
- Functional improvement
- Tolerable side effects

1. The goals of treatment for a patient with chronic pain should be pain reduction (complete absence of pain is probably an unreasonable endpoint), functional improvement, and tolerability of medication side effects.

Chronic Pain Patients

Continue increasing dose of opioid if:

Pain persists

Functional interference persists

Side effects are nil or tolerable

1. With these goals in mind, the dose of opioid medication being used for the treatment of chronic pain should be increased if the pain persists, if functional impairment continues, and if the side effects are nil or tolerable.

Chronic Pain Patients

Differential diagnosis of functional downturn

- Syndrome of opioid abuse/dependence
- Other substance use disorder
- Other psychiatric disorder
- Exacerbation of pain syndrome
- Other medical problem
- Side effect of opioid

1. If the chronic pain patient who has previously been doing well has a downturn in functioning (i.e., worsening pain, poorer functioning), then consider these possibilities to account for this change.
2. For example, it may be the case that the patient has developed a syndrome of opioid abuse or dependence (i.e., addiction to opioids), or another substance use disorder. If such is suspected, then the patient needs to be assessed for such and an appropriate treatment plan created. This may include closer monitoring of the patient, referral to a more intensive level of treatment (such as a program specializing in the treatment of chronic pain and addiction), and/or substance abuse treatment services.

Chronic Pain Patients

Possible side effects of opioids

- Constipation
- Nausea
- Cognitive dysfunction
- Sedation
- Urinary retention
- Pruritus, hives
- Bronchospasm

1. Possible side effects of chronic opioid dosing can include the following. The presence of these may restrict the physician from further dose increases.

Chronic Pain Patients

Benefits of long-acting vs. short-acting opioids

- Steadier serum levels
- Better compliance
- Fewer side effects
- More consistent pain control

1. When selecting an opioid medication for use in the treatment of chronic pain, long-acting opioids are generally better than short-acting ones.

Chronic Pain Patients

Benefits of long-acting vs. short-acting opioids (continued)

Better sleep

Higher patient satisfaction

Less euphoria

Less risk of addiction

Chronic Pain Patients

Long-acting opioids used for baseline pain

Fentanyl-transdermal

Levorphanol – Levo-Dromoran

Methadone – generally given at least tid for analgesia

Morphine – extended release

Oxycodone - extended release

1. Examples of long-acting opioids are the following.
2. Buprenorphine's relatively short duration of analgesic effects makes it a less than optimal medication for use in the treatment of chronic pain. Furthermore, the sublingual form has not been approved for this indication.

Chronic Pain Patients

Short-acting opioids used for breakthrough pain

Codeine

Hydromorphone

Morphine – immediate release

Oxycodone – immediate release

1. The role of short-acting opioids is in the treatment of breakthrough pain. That is, in patients maintained on an opioid for chronic pain, use of these short-acting opioids may be indicated in cases when acute, time-limited pain occurs.

Chronic Pain Patients

Ideal opioid analgesic regimens

Patients without substance abuse disorders:

Long-acting opioid for baseline pain

Short-acting opioid for breakthrough pain

Patients at risk for developing opioid (or other substance) dependence syndrome:

Long-acting opioids only

Chronic Pain Patients

Practical management of patients receiving opioids for chronic pain

Establish treatment contract, which should specify all ground rules including:

- Obtain prescriptions for potentially addictive medications from one physician

- Obtain all prescriptions from one pharmacy

- Take medicines as prescribed, with provisions for fluctuations in pain

1. When arranging treatment with a patient who has chronic pain and who will receive opioids it is useful to set up a contract setting out the terms of the treatment.

Chronic Pain Patients

Practical management of patients receiving opioids for chronic pain (continued)

No premature or after-hours requests for refills

No ED visits for exacerbations of chronic pain

Notify primary MD within 24 hours if additional opioids are obtained

No illicit drug use, as documented by random urine drug screens

Chronic Pain Patients

Practical management of patients receiving opioids for chronic pain (continued)

For all patients, random urine drug screens

For patients with syndrome of opioid dependence,
observed random urine drug screens

Notify all other health care providers about treatment
contract

Receipt of care, as possible, for related medical and
psychiatric problems

Summary

Possible that physicians prescribing buprenorphine for opioid dependence will have chronic pain patients seek them out (especially if the patient is physically dependent on opioids)

Use of opioids for treatment of chronic pain appropriate, and can be safe and effective

Important to recognize appropriate patients for opioids; design and communicate treatment plan and contract

Buprenorphine not presently first choice for chronic pain treatment

1.

Patient Assessment/Selection

Patient Assessment/Selection

Office-based Buprenorphine and Patient Assessment/Selection

The purpose of this section is to provide information on how to assess and select appropriate patients for office-based treatment with buprenorphine. Not all patients who are opioid dependent are good candidates for office-based buprenorphine treatment, and success for both the patient and the practitioner will depend in part on these initial steps of assessment and selection.

- 1.

Outline for This Talk

- I. Identify opioid use/abuse
- II. Establish the diagnosis of opioid dependence
- III. Assess for other conditions
- IV. Determine appropriateness for office-based buprenorphine
- V. Match the treatment plan and treatment resources
- VI. Summary

1. This section provides an overview to the screening and assessment of patients, from the perspective of office-based practice.
2. In general, office-based treatment with buprenorphine will be appropriate if:
 - a) the patient has a diagnosis of opioid dependence,
 - b) if the patient is a good candidate for buprenorphine, and
 - c) if the patient is appropriate for treatment in the office setting (as will be described in more detail in this section).

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1. The process of establishing the diagnosis of opioid dependence begins by identifying patients who are using and abusing opioids.

Identify Opioid Use

Commonly abused opioids

Evaluation of the patient

1. The identification of opioid abuse requires a familiarity with commonly abused opioids.

Commonly Abused Opioids

Diacetylmorphine (Heroin)

Hydromorphone (Dilaudid)

Oxycodone (OxyContin, Percodan, Percocet, Tylox)

Meperidine (Demerol)

Hydrocodone (Lortab, Vicodin)

1. While most patients abuse heroin, there are several other opioids that can be abused. This list is continued on the next slide, and it is not meant to be exhaustive. Note that all of these opioids exert a mu agonist effect.

Commonly Abused Opioids (continued)

Morphine (MS Contin, Oramorph)

Fentanyl (Sublimaze)

Propoxyphene (Darvon)

Methadone (Dolophine)

Codeine

Opium

1.

Commonly Abused Opioids

Opioids are abused by all routes of administration including oral, inhalation, smoking, and injection.

Heroin is most commonly used intravenously, but can be inhaled, smoked, or injected intramuscularly or subcutaneously.

Opium is usually smoked.

The pharmaceutical opioids are usually taken orally (but may also be injected).

1. Furthermore, these opioids can be used via a variety of different routes.
2. Inhalation of opioids is often called “snorting.”
3. Subcutaneous use of opioids is often called “skin popping” or simply “popping.”

Commonly Abused Opioids

Common street names for heroin:

horse

chiva

junk

skag

smack

boy

H

1. When interviewing a patient for possible opioid abuse and dependence, it can be useful to recognize that there are a variety of street names used to identify heroin. Street names vary from place to place and from time to time. Shown here are examples of some names used for heroin.
2. While heroin can be called “boy,” cocaine is often called “girl.”

Commonly Abused Opioids

Other street names:

Morphine: M, Miss Emma

Hydromorphone: DLs (for Dilaudid)

Oxycodone: Percs (for Percocet)

Methadone: Done or Dolly's (for Dolophine)

1. Besides these street names for heroin, there are also street names for other abused opioids.

Identify Opioid Use

Commonly abused opioids

Evaluation of the patient

1. Identifying opioid use by a patient then leads to the need for further evaluation.

Evaluation of the Patient

Attitude of the interviewer:

Matter-of-fact, non-judgmental, curious, respectful,
interested, professional, focused on taking a good medical
history

1. When evaluating the patient who is suspected (or known) to abuse opioids, the interviewer should assume a matter-of-fact, professional attitude. The focus should be on obtaining a good medical history, with particular focus on areas relevant to the person who has been abusing opioids.
2. The following slides provide more detail about topics and areas that should be covered in this evaluation of the patient.

Evaluation of the Patient

History of drug use:

Start with first substance used

Ask about all substances (including licit and illicit)

Determine changes in use over time (frequency, amount, route)

Assess recent use (past several weeks)

1. The interviewer should begin with the first substance used, and then move forward in time asking about the progression in the patient's drug use.
2. All substances, including caffeine and nicotine, should be covered.
3. Determine how the pattern of drug use has changed over time – with respect to frequency, amount, route of administration, and acute response to the effects of the drug.
4. Ask about recent use, including use in the weeks and days just prior to the assessment.

Evaluation of the Patient

Tolerance, intoxication, withdrawal:

Explain what is meant by tolerance

Determine the patient's tolerance and withdrawal history

Ask about complications associated with intoxication and withdrawal

1. It may be necessary to explain to the patient what is meant by tolerance (i.e., that greater amounts of the drug are needed to achieve the same effect, or that there is a diminished effect from the same amount of drug).
2. Determine if there have been complications with intoxication (e.g., falls) or withdrawal (e.g., seizures).

Evaluation of the Patient

Relapse/attempts to abstain:

Determine if the patient has tried to abstain, and what happened

Ask what was the longest period of abstinence

Identify triggers to relapse

1. Patients may have attempted to abstain on their own (go “cold turkey” in the case of opioids). Exploring such episodes, and the results, can be useful (in terms of the severity of resultant withdrawal symptoms, motivation of the patient, and previous episodes of success with abstinence).
2. Ask what triggers lead to relapse after a period of abstinence.

Evaluation of the Patient

Consequences of use:

Determine current and past levels of functioning

Identify consequences to drug/alcohol use (such as):

Medical

Family

Employment

Legal

Other

1. Help patients to assess the consequences of their drug use. Determine their current level of psychosocial functioning (e.g., relationship with family, employment), and their past level of functioning. Identifying losses in their life may increase or bolster the motivation to change.
2. Examples of medical consequences can include hepatitis, HIV infection, and other infections (e.g., endocarditis, abscesses). These are discussed further in the medical co-morbidity section.
3. Examples of family consequences can include separation or divorce, and estrangement from parents, siblings, and children.
4. Examples of employment consequences can include loss of job, loss of job skills, and loss of license.
5. Examples of legal consequences can include incarceration, parole or probation, and loss of custody of children.

Evaluation of the Patient

Craving and control:

Ask if the patient experiences craving to use and/or a compulsive need to use

Determine if patient sees loss of control over use

1. Patients who have become dependent on drugs or alcohol often report a subjective desire or hunger to use – a craving – that can be overwhelming at times. Along with this subjective state can be the behavioral component – a compulsive need to use drugs or alcohol.

Evaluation of the Patient

Substance abuse treatment history:

Treatment episodes (detoxifications – medically and non-medically supervised; maintenance; counseling)

Response following each treatment intervention

Attendance at 12 step (or other self-help) meetings

1. The patient's substance abuse treatment history can help to determine the length and severity of the addiction.
2. Assessing a patient's involvement with self-help meetings, such as Alcoholics Anonymous (AA) or Narcotics Anonymous (NA), can provide another indicator of the patient's level of motivation. You can ask:
 - a) how many meetings did he/she attend per week; for how many weeks (more meetings per week indicates a higher motivation; 90 meetings in 90 days is frequently recommended);
 - b) did the patient get a sponsor (if so, it is an indication that he/she was more highly motivated to make the self-help program effective).

Evaluation of the Patient

Psychiatric history:

Inpatient and/or outpatient treatment episodes

Untreated episodes of psychiatric illness

Treatment with psychiatric medications

1. The patient should be assessed for a past psychiatric history. Questions should not be limited to treatment delivered by a psychiatrist or occurring at an inpatient or outpatient setting. Psychiatric treatment may have been delivered by non-psychiatrists (e.g., an antidepressant prescribed by a family physician, psychotherapy provided by a psychologist), and the assessment should include this possibility.

Evaluation of the Patient

Medical history:

Past and/or present:

Significant medical illnesses

Hospitalizations

Operations

Accidents/injuries

Drug allergies

Current medications

1. The medical history should include significant medical illnesses (both acute and chronic), as well as operations, accidents, medications and allergies. Questions should be sure to include assessment of the medical consequences of drug use, such as infectious illnesses (hepatitis, HIV, abscesses).
2. It can be useful to ask if the patient sees a relationship between the drug use/abuse and the medical conditions.
3. Current medications should include both prescription as well as over the counter medications (including dietary supplements).

Evaluation of the Patient

Family history:

- Substance abuse disorders
- Other psychiatric conditions
- Other medical disorders

1. The family history can provide information about vulnerabilities the patient may have (both in their developmental history, as well as genetically).

[Reference:

Pickens R.W., Svikis D.S. (eds) Biological Vulnerability to Drug Abuse. NIDA Research Monograph 89, U.S. Department of Health and Human Services, National Institute on Drug Abuse, Rockville, Maryland, 1988.]

Evaluation of the Patient

Personal (or social) history:

- Birth and early development
- Education
- Employment and occupations
- Marital status and children
- Living situation
- Legal status

1. The personal (or social) history provides information about other areas that may influence to the patient's drug use or ability to achieve and maintain abstinence.
2. For example, active drug use by a partner or other member of the household may make it difficult for the patient to maintain abstinence. Lack of employment may provide the patient with unstructured time, increasing risk of use.

Outline for This Talk

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VI. Summary

1. After identifying that a patient is abusing opioids, the next step is to determine if the patient has the diagnosis of an opioid dependence syndrome. The most common and well accepted means for doing this is to apply diagnostic criteria, and the following slides review the DSM-IV criteria for a diagnosis of any substance dependence (including opioids).
2. It is not known at the present time if federal rules/regulations will require that patients be opioid dependent to be treated with buprenorphine, or if exceptions will be possible.
3. It may be the case that patients who abuse opioids (but are not dependent) may be appropriate for buprenorphine treatment – for example, if they have a high risk of progression to dependence, or are injecting opioids.
4. There could also be patients who are not currently using opioids, but who are nonetheless good candidates for buprenorphine treatment – for example, patients with a history of good response to buprenorphine, who have had their medication discontinued (e.g., incarceration), and are now at high risk for relapse when released from prison/jail.
5. Thus, while a diagnosis of opioid dependence will probably be the most common scenario, it is possible that some patients may be considered for buprenorphine treatment even though they do not have a current diagnosis of opioid dependence.

DSM-IV Criteria for Opioid Dependence

A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12-month period:

1. Tolerance, as defined by either of the following:
 - a) a need for markedly increased amounts of the substance to achieve intoxication or the desired effect, or
 - b) markedly diminished effect with continued use of the same amount of the substance

1. This and the following slides list the DSM-IV criteria for dependence on a psychoactive substance. The criteria are generic – that is, they apply to all substances, including opioids.

[Reference:

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. American Psychiatric Association, Washington, D.C., 1994.]

DSM-IV Criteria for Opioid Dependence

2. Withdrawal, as manifested by either of the following:
 - a) the characteristic withdrawal syndrome for the substance, or
 - b) the same (or closely related) substance is taken to relieve or avoid withdrawal symptoms

1. Note that the criteria tolerance and withdrawal relate to physical dependence on the substance. A patient can fulfill the criteria for a syndrome of dependence without necessarily having evidence of physical dependence. That is, patients can have three or more of the DSM-IV criteria, but not the first or second, and thus qualify for the diagnosis of dependence.

2. Also, note that tolerance and withdrawal cannot be applied toward a diagnosis of opioid dependence unless use of the drug is maladaptive. For example, evidence of tolerance and/or withdrawal associated with use of prescribed opioids for chronic pain are not included in making a diagnosis of opioid dependence unless the patient is using the prescribed opioids in a maladaptive way.

DSM-IV Criteria for Opioid Dependence

3. The substance is often taken in larger amounts or over a longer period than was intended
4. There is a persistent desire or unsuccessful efforts to cut down or control substance use
5. A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects

1.

DSM-IV Criteria for Opioid Dependence

6. Important social, occupational, or recreational activities are given up or reduced because of substance use
7. The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance

DSM-IV Criteria for Opioid Dependence

Diagnosis can include modifiers indicating if the patient is physiologically (or physically) dependent on the substance (i.e., has evidence of tolerance or withdrawal), is in various stages of remission, is on agonist treatment, or is in a controlled environment

DSM-IV Criteria for Opioid Abuse

Criteria for abuse of any substance, including opioids:

1. A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one (or more) of the following, occurring within a 12-month period:
 - a) recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home

1. Patients who don't fulfill criteria for dependence may fit the criteria for Opioid Abuse (less severe form of pathological use).

DSM-IV Criteria for Opioid Abuse

Criteria for abuse (continued):

- b) recurrent substance use in situations in which it is physically hazardous
- c) recurrent substance-related legal problems
- d) continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance

The criteria for abuse of any substance, including opioids:

1. A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one (or more) of the following, occurring within a 12-month period:
 - a) recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home
 - b) recurrent substance use in situations in which it is physically hazardous
 - c) recurrent substance-related legal problems
 - d) continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance
2. The symptoms have never met the criteria for Substance Dependence for this class of substance.

DSM-IV Criteria for Opioid Abuse

Criteria for abuse (continued):

2. The symptoms have never met the criteria for Substance Dependence for this class of substance.

The criteria for abuse of any substance, including opioids:

1. A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one (or more) of the following, occurring within a 12-month period:
 - a) recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home
 - b) recurrent substance use in situations in which it is physically hazardous
 - c) recurrent substance-related legal problems
 - d) continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance
2. The symptoms have never met the criteria for Substance Dependence for this class of substance.

Opioid Physical Dependence

Important Clinical Features of Opioid Physical Dependence

Physical dependence can occur after relatively short periods of daily use (e.g., 2 weeks)

Opioid physical dependence is characterized by regular administration to avoid withdrawal

1. The development of physical dependence on opioids depends upon the type of opioid being used, the frequency it is used, and the length of time that it has been used. While physical dependence is generally indicated by the presence of a withdrawal syndrome upon cessation (or a reduction) in use, it can also be shown by the acute administration of an opioid antagonist such as naloxone (which precipitates a withdrawal syndrome). Studies have shown that administration of a large dose of an opioid antagonist to someone who has used only one or a few doses of an opioid can precipitate withdrawal. This suggests that the development of physical dependence begins after the first few doses of an opioid. However, for clinical purposes it is likely patients will not experience spontaneous withdrawal until they have used opioids on a daily (or near daily) basis for about two weeks.
2. Patients often report that they began using opioids to get a high feeling (that the positive effects were what drove continued use), but that sustained use was driven by the need to feel normal. (“I started using to get high but now I have to use to feel OK.”) This is related to the desire to avoid the unpleasant symptoms of spontaneous opioid withdrawal.

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1. A diagnosis of opioid dependence is necessary for treatment with buprenorphine (with the possible exceptions noted earlier). However, in addition to the diagnosis of opioid dependence, assessment for other conditions should also be conducted.

Assess for Other Conditions

Other substance use, abuse, dependence

Medical co-morbidity

Psychiatric co-morbidity

1. These other conditions include other substance use, as well as medical and psychiatric co-morbidity. The results from these assessments will help guide in the determination of the suitability of the patient for office-based buprenorphine treatment.
2. We will begin by talking about other substance use, abuse, and dependence.

Other Substance Use, Abuse, Dependence

Reason to assess for other substance use

Detecting other substance use

Types of other substance use

1. There are several important reasons to screen for other substance use disorders in patients with opioid dependence.

Other Substance Use, Abuse, Dependence

Reason to assess for other substance use

Co-morbid substance use disorders are common in patients with opioid dependence

Important to assess when initially evaluating the patient, as their presence/absence can guide whether or not office-based treatment is appropriate

1. It is quite common to find co-morbid substance use disorders in patients with opioid dependence.
2. Especially common is abuse of cocaine, cannabis, sedative-hypnotics (e.g., benzodiazepines), and alcohol. These will be discussed in more detail in a moment.
3. The severity of use may be dependence (i.e., fulfilling the criteria listed earlier, but for another drug class), abuse (a less severe form of problematic use versus dependence), or occasional, sporadic use (i.e., early use that does not significantly impact the patient's functioning).
4. Concurrent use/abuse/dependence can be a prominent factor in the final determination of the patient's suitability for office-based treatment. More intensive treatment resources may be needed to address this other drug or alcohol use.

Other Substance Use, Abuse, Dependence

Reason to assess for other substance use

Detecting other substance use

Types of other substance use

1. There are several possible ways to screen and detect other substance use.
2. Note that the patient may minimize self-reported use of other drugs or alcohol, since he or she may realize that a pattern of abuse or dependence may result in failure to qualify for office-based treatment.
3. Failure to detect use, or appreciate the severity of use, may lead to increased time and effort with the patient once he/she is fully engaged in office-based buprenorphine treatment.

Other Substance Use, Abuse, Dependence

Detecting substance use

Screening instruments

Self-report of use, reason

Multiple trauma

Hospitalization

Infections

1. There are a large variety of screening instruments available. While many of these are primarily for alcohol abuse/dependence, some have been adapted for drug use.
2. Screening for alcohol abuse is important in and of itself, and may serve as a signal that the patient is using alcohol and/or drugs other than opioids. Examples of substance abuse screening instruments include: DAST (Drug Abuse Screening Test), AUDIT (Alcohol Use Disorders Identification Test), CAGE, CAGE-AID, MAST (Michigan Alcohol Screening Test), Short MAST, MAST-G (Geriatric version), Skinner Trauma Screen, and the TWEAK.
3. Self-reported use is important to assess as well – ask the patient about drug use. You can begin by asking about smoking tobacco, then patterns of alcohol use. This can be followed by asking about cannabis use, then other illicit drug use.
4. While the candidate for buprenorphine treatment has already been identified as having a drug problem, it is useful to note here that, in general, the practitioner should have an increased suspicion of drug use in any patient with a history of multiple traumas, frequent hospitalizations, and recurrent or particular types of infections. These events may indicate drug and/or alcohol use not previously diagnosed.

Other Substance Use, Abuse, Dependence

Detecting substance use (continued)

- Track or puncture marks
- Infection (abscesses, cellulitis)
- Constricted pupil (opioid intoxication)
- Dilated pupil (opioid withdrawal)
- Confusion, disorientation

1. In addition to self-reported use, objective information can help in patient identification and/or determination of the severity and history of use. This information primarily comes from the physical examination of the patient.
2. The signs listed in the slide are evidence of opioid effects. In addition, cocaine effects can also be detected on the physical examination. For example, a constricted pupil can be due to cocaine withdrawal, and a dilated pupil to cocaine intoxication.

Other Substance Use, Abuse, Dependence

Detecting substance use (continued)

Laboratory methods:

Blood

Urine

Hair

1. Certain lab test results can raise suspicion for drug use; for example, liver function test abnormalities; elevated mean corpuscular volume on CBC; GGTP elevation; carbohydrate-deficient transferrin can indicate alcohol use/abuse; indicators of hepatitis infection (e.g., B and C antibodies), and being HIV antibody positive can indicate injection drug use.
2. Urine testing for the presence of drugs of abuse (morphine indicating heroin use; benzoylecgonine indicating cocaine use; other drugs of abuse such as cannabis and benzodiazepines) can also be useful in assessing the patient. However, recognize that if the use is sporadic, the patient may not have used near the time the sample is obtained. Sporadic use may result in a negative urine sample.
3. Hair testing may eventually be useful in screening (especially for more sporadic patterns of drug use), but its current clinical usefulness should be considered limited and primarily experimental.

Other Substance Use, Abuse, Dependence

Reason to assess for other substance use

Detecting other substance use

Types of other substance use

1. Finally, let's take a moment and discuss the types of other substance use that may be seen in opioid dependent patients.
2. The management of use of other drugs, such as cocaine and marijuana, is discussed in other sections. The physician's approach will depend upon treatment philosophy, available resources, and the particular patient.

Other Substance Use, Abuse, Dependence

Types of other substance use

Alcohol

Sedative-hypnotics

Cocaine

Cannabis

1. In a study of opioid dependent people (n=716) seeking methadone treatment the following rates (%s) of co-morbid substance use disorders were found:

	<u>lifetime</u>	<u>current</u>
cocaine dependence	64.7	40.2
cocaine abuse	12.4	3.4
cannabis dependence	50.8	16.2
cannabis abuse	14.9	2.4
alcohol dependence	50.3	24.7
alcohol abuse	13.0	1.8
sedative-hypnotic abuse	13.0	1.5

2. Alcohol dependence may require inpatient or residential detoxification so the patient can be monitored by health care personnel, especially if other medical problems are present.

3. Continuing abuse or dependence on CNS depressants (alcohol, sedative-hypnotics) should be considered a relative contraindication to buprenorphine use. Reports of deaths associated with the combination of buprenorphine and benzodiazepines have come from France. These cases may be limited to IV use of buprenorphine and benzodiazepines, and no reports of such events have come from the outpatient studies done in the U.S. However, caution in prescribing buprenorphine to patients abusing CNS depressants is warranted.

[Reference: Brooner R.K., King V.L., Kidorf M., Schmidt C.W., Bigelow G.E. Psychiatric and substance use comorbidity among treatment-seeking opioid abusers. Arch Gen Psychiatry 54:71-80, 1997.]

Assess for Other Conditions

Other substance use, abuse, dependence

Medical co-morbidity

Psychiatric co-morbidity

1. It is also important to assess for co-morbid medical disorders when initially evaluating the patient. These are reviewed in detail in the Medical Co-morbidity section.

Co-morbid Medical Disorders

Important to assess for such, since (like other co-morbid disorders), their presence can influence the decision to provide office-based treatment of opioid dependence

Advantage: One-stop treatment for opioid dependence and other medical needs

Disadvantage: Management of co-morbidity can be complicated and require specialized services

1. Office-based treatment for opioid dependence provides an opportunity to integrate the treatment of substance abuse and other medical disorders.
2. On the other hand, patients with complicated medical problems, or multiple medical disorders, may be better treated at more intensive treatment sites (e.g., a clinic that specializes in treatment for patients with HIV infection).
3. The decision on whether to treat or refer, based upon the presence of co-morbid medical problems, will need to be based upon the availability and range of medical services that exist within the office-based site, as well as the comfort level of the practitioner in managing patients with opioid dependence and other medical problems.

[References:

O'Connor P.G., Oliveto A.H., Shi J.M., Triffleman E.G., Carroll K.M., Kosten T.R., Rounsaville B.J., Pakes J.A., Schottenfeld R.S. A randomized trial of buprenorphine maintenance for heroin dependence in a primary care clinic for substance users versus a methadone clinic. *Am J Med* 105:100-5, 1998.

O'Connor P.G., Oliveto A.H., Shi J.M., Triffleman E., Carroll K.M., Kosten T.R., Rounsaville B.J. A pilot study of primary-care-based buprenorphine maintenance for heroin dependence. *Am J Drug Alcohol Abuse* 22:523-31, 1996.]

Co-morbid Medical Disorders

Separate section on this topic

Not uncommon to find infectious, sexually transmitted, and liver diseases; nutritional problems; lung diseases secondary to smoking; and consequences of alcohol use

1. Patients with complicated medical problems, or multiple medical disorders, may be better treated at more intensive treatment sites.

2. The Review of Systems should include the following areas that are particularly pertinent to patients with substance abuse disorders:

Skin: track marks, cellulitis

Infectious Diseases: TB, +PPD, HIV, hepatitis (A,B,C,D, etc.), syphilis, PID, STDs

Obstetric-Gyn: amenorrhea, pregnancy, ob complications, spontaneous abortion

Cardiovascular: arrhythmia, cardiomyopathy, heart murmur, endocarditis, pericarditis, thrombophlebitis, mycotic aneurysm

Gastrointestinal: hepatitis, cirrhosis

Hematologic: anemia, thrombocytopenia

Pulmonary: pulmonary edema, COPD, chronic cough, pneumonia

Immune Function: lymphadenopathy, lymphocytosis

Nutrition: vitamin/mineral deficiency, malnutrition

Musculoskeletal: osteomyelitis, septic arthritis, aseptic necrosis

Neurologic: brain, epidural or subdural abscess, fungal meningitis, stroke, neuropathy

Trauma: motor vehicle accident, pedestrian accident

Assess for Other Conditions

Other substance use, abuse, dependence

Medical co-morbidity

Psychiatric co-morbidity

1. Like patients who are medically complicated, the presence of psychiatric co-morbidity can influence the decision of whether or not to treat a patient in your office. Co-morbid psychiatric conditions are commonly found in patients with opioid dependence.

Co-morbid Psychiatric Disorders

Separate section on this topic

Most common to find depression, anxiety and personality disorders

Important to assess for such, since (like co-morbid substance use disorders), their presence can influence the decision to provide office-based treatment of opioid dependence

1. The presence of co-morbid psychiatric disorders may lead to the decision to refer the patient to a more intensive treatment site (e.g., inpatient treatment, a methadone clinic), rather than attempting office-based treatment with buprenorphine.
2. Psychiatrists may be quite willing to treat opioid dependent patients with co-morbid psychiatric disorders in their office, but prefer not to treat opioid dependent patients with co-morbid medical disorders. Similarly, internists and family practitioners may be quite willing to treat opioid dependent patients with co-morbid medical disorders in their office, but prefer not to treat opioid dependent patients with co-morbid psychiatric disorders. Different types of practices will need to develop expertise and experience in the particular types of patients they treat. Target treatment populations should be in the area of the physician's general expertise.

Co-morbid Psychiatric Disorders

Certain psychiatric problems that present at the time of initial assessment are relative contraindications to the initiation of office-based buprenorphine treatment. For example, patients actively psychotic or who have active suicidal or homicidal ideation should not be started on buprenorphine under most circumstances.

1. While patients who are actively psychotic or have active suicidal or homicidal ideation should not be started on buprenorphine under virtually any circumstances, an exception might be acute hospitalization to stabilize their psychiatric problem and concurrently start buprenorphine treatment, followed by return for office-based buprenorphine treatment.
2. Significant psychiatric distress and disorder that presents at the time of initial assessment for office-based buprenorphine treatment should result in strong consideration of referral to a more intensive treatment service, such as a dual diagnosis program.

Outline for This Talk

- I. Identify opioid use/abuse
- II. Establish the diagnosis of opioid dependence
- III. Assess for other conditions
- IV. Determine appropriateness for office-based buprenorphine**
- V. Match the treatment plan and treatment resources
- VI. Summary

1. After determining the patient is opioid dependent, and screening for co-existing conditions, the physician should make a determination of the appropriateness of the patient for office-based buprenorphine treatment.

Appropriateness for Office-based Buprenorphine

Factors to keep in mind when considering a patient for office-based buprenorphine treatment

Factors indicating the patient is less likely to be an appropriate candidate for office-based buprenorphine treatment

1. We'll begin by looking at questions to keep in mind when considering a patient for office-based buprenorphine treatment. These are also discussed in more detail in the Buprenorphine Guidelines document.

Appropriateness for Office-based Buprenorphine

Consider these factors

1. Does the patient have a diagnosis of opioid dependence?
2. Is the patient interested in office-based buprenorphine treatment?
3. Does the patient understand the risks/benefits of buprenorphine treatment?

1. If the patient qualifies for buprenorphine treatment, is he/she interested in it? The patient should understand the other treatment options available.
2. Does the patient understand the risks and benefits of buprenorphine treatment? Does he/she understand that the medication is not a silver bullet, that it will address some aspects of their substance abuse (such as withdrawal, suppression, and blockade), but not all aspects (such as triggers and cravings that may be elicited by events and circumstances in the environment)?

Appropriateness for Office-based Buprenorphine

Consider these factors (continued)

4. Is he/she expected to be reasonably compliant?
5. Is he/she expected to follow safety procedures?
6. Is the patient psychiatrically stable?

1. Is the patient expected to be reasonably compliant? Are there indicators from their life that suggest they are reliable (such as steady employment, following through in taking medications for other medical conditions, showing up on time for their appointments at the office)?

Appropriateness for Office-based Buprenorphine

Consider these factors (continued)

7. Are the psychosocial circumstances of the patient stable and supportive?
8. Can the office provide the needed resources for the patient (either on or off site)?
9. Is the patient taking other medications that may interact with buprenorphine?

1. Does the patient have supports that will aid in the treatment (such as spouse, significant other, friend who doesn't use drugs)? Does the patient have stable and safe housing?
2. Are there resources available via the office to provide appropriate treatment for the patient? Are there other physicians in the group practice? Are there treatment programs that will accept referral for more intensive levels of service?
3. Is the patient taking other medications that may interact with buprenorphine (such as naltrexone, benzodiazepines, or other sedative-hypnotics)?

Appropriateness for Office-based Buprenorphine

Factors to keep in mind when considering a patient for office-based buprenorphine treatment

Factors indicating the patient is less likely to be an appropriate candidate for office-based buprenorphine treatment and should be referred elsewhere

1. In addition to these questions, there are some factors that indicate the patient is less likely to be an appropriate candidate for office-based buprenorphine treatment.

Appropriateness for Office-based Buprenorphine

Patient is less likely to be an appropriate candidate for office-based buprenorphine treatment

1. Dependence on high doses of benzodiazepines, alcohol, or other CNS depressants
2. Significant psychiatric co-morbidity
3. Active or chronic suicidal or homicidal ideation or attempts

1. Several of these points have been reviewed earlier and/or are covered in more detail in other sections, but are worth repeating here. Additional points continue on the next slides.

2. These factors should be considered relative rather than absolute contraindications for office-based buprenorphine treatment. That is because there are circumstances where office-based buprenorphine treatment may be attempted even though the patient has one or more of these factors. For example, patients who are also alcohol dependent may undergo detoxification and then engage in office-based buprenorphine treatment along with continued care for their alcohol dependence. Under such circumstances special treatment plans can be generated, highly supportive family members might be enlisted, and efforts might be made because no other treatment services are available locally.

Appropriateness for Office-based Buprenorphine

Patient is less likely to be an appropriate candidate for office-based buprenorphine treatment (continued)

4. Multiple previous treatments and relapses
5. Non-response to buprenorphine in the past
6. High level of physical dependence (risk for severe withdrawal)
7. Patient needs cannot be addressed with existing office-based resources

1. Patients who have evidence of a high level of physical dependence (e.g., use large amounts of heroin on a daily basis) may not be optimal candidates for buprenorphine treatment, since buprenorphine appears to produce a maximal opioid agonist effect equivalent to approximately 60 mg of daily methadone. Patients who report severe withdrawal when they do not use an opioid may not be good candidates for buprenorphine, especially induction on to buprenorphine in an office-based setting.

Appropriateness for Office-based Buprenorphine

Patient is less likely to be an appropriate candidate for office-based buprenorphine treatment (continued)

8. High risk for relapse
9. Pregnancy
10. Current medical condition(s) that could complicate treatment
11. Poor support systems

1. Medical conditions that may be relative contraindications to buprenorphine treatment include:

- a) seizures (caution should be exercised since buprenorphine and anticonvulsant medications may interact)
- b) HIV and STDs (caution should be exercised since buprenorphine and antibiotic and/or antiviral medications may interact)
- c) hepatitis/impaired hepatic function (buprenorphine is not contraindicated in patients with mild elevations of liver function tests, but active hepatitis and higher elevations of liver function tests should be evaluated and treated appropriately; closer monitoring of the patient, response to buprenorphine, and liver function tests is indicated when the patient has evidence of more severe impaired hepatic function)

2. The topic of pregnancy and opioid dependence treatment is covered in the section on special treatment populations. Methadone is the current standard of care for treating pregnant women who are opioid dependent. Studies of buprenorphine in pregnancy are currently being conducted, but use of buprenorphine in pregnant women should be considered investigational at this time.

3. For patients who are not suitable candidates for office-based buprenorphine treatment, referral to a more comprehensive and/or intensive treatment site should be made.

Outline for This Talk

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1. Are the treatment objectives for the patient achievable with the resources available through the setting of office-based treatment? Not all resources need to be on-site, but the office must be able to refer and follow treatment that occurs off-site.

Match Treatment Plan and Resources

Determine appropriateness of patient for office based buprenorphine treatment by considering the needs of the patient and the available resources

ASAM patient placement criteria can help guide

Acute intoxication/withdrawal potential

Biomedical conditions, complications

Emotional/behavioral/cognitive conditions and complications

1. When considering the treatment of an opioid dependent patient with buprenorphine delivered via the office, it may be useful to consider the ASAM Patient Placement Criteria (ASAM PPC) to organize the final decision making. These criteria, shown here and continued on the next slide, are based upon six dimensions developed by the American Society of Addiction Medicine (ASAM) for use in determining the treatment placement of patients with substance abuse disorders.

[Reference:

American Society of Addiction Medicine. Patient Placement Criteria for the Treatment of Substance-Related Disorders, Second Edition (ASAM PPC-2), American Society of Addiction Medicine Chevy Chase, Maryland, 1996.]

Match Treatment Plan and Resources

ASAM patient placement criteria can help guide (continued)

Readiness to change

Continued use or continued problem potential

Recovery environment

Can the needs of the patient be addressed by available resources?

1. The final decision is whether or not the needs of the patient can be addressed by the available resources. An analogy may be useful: A surgeon would not plan an outpatient operative procedure on a patient who has significant co-morbid problems and is medically unstable. A more intensive level of service would be used (e.g., inpatient treatment). The needs of the patient would be matched to the treatment capacity or resources by the surgeon.

Furthermore, even if the patient appeared relatively uncomplicated, the responsible surgeon would not conduct the outpatient procedure before learning of the inpatient resources available in case there were complications to the outpatient procedure.

Therefore, the treatment of the opioid dependent patient should follow a similar logic. The decision to provide treatment from the office should be based upon the suitability of the patient for this level of service and the availability of other resources in case complications in the office-based treatment arise.

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Summary

Determination of suitability for office-based buprenorphine treatment begins with the presence of a diagnosis of opioid dependence

In addition, many patient factors (such as co-morbid conditions) will guide the decision of whether or not to treat in the office with buprenorphine

Final decision is whether the patient's needs can be addressed by the resources available through the office

Clinical Management

Clinical Management:
Interactions with the Patient

Clinical management encompasses a wide variety of subjects, and many of these are addressed in other sections (such as the assessment of co-morbid conditions, the importance of consent, and the evaluation for a diagnosis of opioid dependence).

1. All of the sections of this curriculum are, in a sense, variations on the theme of patient management. For purposes of this talk, three areas are singled out for attention: interactions with the patient, urine testing, and managing problematic behaviors. These elements should be designed to create a therapeutic structure for the clinician's interactions with the patient.

The purpose of this section is to review a variety of clinical interactions with the patient in office-based buprenorphine treatment. The clinical situations and problematic behaviors reviewed here range from the routine to the rare. However, all share the common feature of being possible – and thus require the clinician to have considered in advance how to respond to their occurrence.

- 1.

This section stresses the importance of anticipation and preparation, so the clinician is not making sudden decisions about how to handle a situation and so the response can be in line with therapeutic principles and treatment goals. Advance preparation is important not only for responses to problematic behaviors, but also for responses to more routine clinical situations.

1. It is important to stress that many of the situations reviewed in this talk are extremely rare occurrences – especially if the clinician is treating relatively stable patients. It is equally important to note that the situations reviewed in this talk could occur with patients treated for conditions other than opioid dependence.
2. However, being prepared is the take-home point here. By being prepared, the clinician and the clinician's office staff will be better able to handle a problematic situation in a way that is therapeutic for the patient.

Outline for This Talk

- I. Interactions with the patient
- II. Urine testing
- III. Managing problematic behavior
- IV. Summary

1. There are three topics that will be covered in this talk.

Outline for This Talk

- I. Interactions with the patient
- II. Urine testing
- III. Managing problematic behavior
- IV. Summary

1. We will begin with a discussion on interactions with the patient.

Interactions with the Patient

The initial visit with the patient

Rules and expectations

Boundaries in patient-staff interactions

1. Specifically, we're going to address three aspects of interacting with the patient: the initial visit with the patient, the rules and expectations (including how to communicate them to the patient, and what the rules and expectations can include), and the importance of maintaining boundaries in patient-staff interactions.
2. We'll start by talking about the initial visit with the patient.

[Reference:

Glezen L.A., Lowery C.A. Practical issues of program organization and operation. In: Strain E.C., Stitzer M.L. (eds), Methadone Treatment for Opioid Dependence. Johns Hopkins University Press, Baltimore, Maryland, 1999; pages 237-40.]

The Initial Visit with the Patient

Establish foundation of trust at first visit

Relationship in which patient can be open and confident that he/she can report difficulties

Physician must be open, understanding, and willing to listen – straightforward and non-judgmental

1. Several topics should be reviewed at the time of the initial visit, and the physician should have several goals in mind for this first interaction. These topics and goals are listed on this and the next slides.
2. The first visit is critical to the patient's success. Key to this visit is the establishment of a foundation of trust.
3. It will aid in the management of the patient if the patient can confide in you the status of the drug use. This can help in determining what services are indicated.
4. In order to establish trust, the physician should strive to be open, understanding, and willing to listen to the patient. The physician's attitude should be straightforward, matter-of-fact, and non-judgmental.

The Initial Visit with the Patient

Be prepared for defensiveness

Address concerns about disclosure, confidentiality

Start the interview with questions not likely to increase defensiveness

Use open-ended or quantifiable rather than “yes-no” questions

Assumptive questioning may yield more accurate responses

1. When interviewing the patient, the physician should be prepared for defensiveness on the part of the patient.
2. Early in the interview, the physician should address issues of confidentiality and disclosure (which are reviewed in the section on Patient Confidentiality).
3. Initial questions in the first interview should be open-ended and avoid increasing the defensiveness of the patient. Later in the interview, questions may become more focused and, at times, can contain an element of assumption. (For example, “When was the last time you were high?” “How many times did you use this past week?”)
4. The overall goals of the first interview are to obtain accurate information from the patient while establishing a therapeutic relationship.

[Reference:

Schottenfeld R.S., Pantalon M.V. Assessment of the Patient (Chapter 12). In: Galanter M., Kleber H.D. Textbook of Substance Abuse Treatment, Second Edition. American Psychiatric Press, Washington, D.C., 1999.]

The Initial Visit with the Patient

Part of the initial visit is to review rules and expectations with the patient, making sure that the patient understands them

During the patient's first visit, give him/her copy of the rules and expectations to take home

1. The rules and expectations will be reviewed in the next section.

Interactions with the Patient

The initial visit with the patient

Rules and expectations

Boundaries in patient-staff interactions

1. Next, let's talk about specific rules and expectations that should be conveyed to the patient.

Rules and Expectations for the Patient

General principles for rules and expectations

Example items addressed in rules and expectations

Conveying rules and expectations

1. There are three aspects of the rules and expectations that will be reviewed. We'll begin with general principles for rules and expectations.

Rules and Expectations for the Patient

General principles for rules and expectations

Provide clear guidelines and expectations for patients

Help staff understand operation of office

Lay the groundwork for confronting patients about problematic behaviors

1. The rules and expectations should be clear guidelines that are conveyed at the time of the initial assessment of the patient – before buprenorphine treatment is initiated. A part of the assessment is determining that the person can comply with the rules, that medication will be taken as prescribed, and that it will be kept safe.
2. In addition to helping the patient, clear guidelines also can serve a useful purpose for office staff – conveying to staff how patients should be managed, and how you will respond to potential problems in treating opioid dependent patients. Input from staff should be elicited when developing rules and expectations.
3. Having rules and expectations in place lays the necessary groundwork for confronting patients about problematic behaviors. It avoids the problem of having the patient say he/she did not know the consequences to certain acts.

Rules and Expectations for the Patient

General principles for rules and expectations

Examples of items addressed in rules and expectations

Conveying rules and expectations

1. Next, let's review some examples of items that could be included in a set of rules and expectations. Unique aspects of each office will govern particular items included in a set of rules and expectations.

Rules and Expectations for the Patient

Examples of items addressed in rules and expectations

Treatment philosophy

Prescription procedures

Safe and proper storage of medication

1. In addition to specific items, the rules and expectations can also include more general items (such as the physician's philosophy of treatment for substance abuse). The treatment philosophy could state the physician's belief about the nature of substance abuse (e.g., that it is a chronic medical disorder that responds best when treated with medications combined with non-pharmacological treatments), the goal of treatment (e.g., abstinence), and the proper approach to treating patients (e.g., with dignity and respect).
2. Details of the prescription procedures can include an explanation of the role of the physician, the office staff, and the patient in the handling of prescriptions. The rules and expectations can explain the maximum number of days medication will be provided with a prescription, how the physician manages lost buprenorphine prescriptions, and the dosing of medication on site (e.g., for the first few days of induction) versus at home (i.e., after stabilization on a maintenance dose).
3. The physician should determine whether the patient can be expected to store the medication safely, e.g., in a safe place inaccessible to children and other household members.

Rules and Expectations for the Patient

Example items addressed in rules and expectations (continued)

Proper adherence to induction and maintenance protocols

Need for full and prompt disclosure of non-prescriptive psychoactive substances

Reporting of other prescriptive medications

1. The patient should not adjust medication unilaterally. Alterations in dose should only be made after consulting with the physician.
2. The physician should explain that illicit drug use and/or problematic alcohol use needs to be reported to the physician. Use should not automatically result in discharge from treatment, but will require a change in the treatment plan (e.g., adjustment in buprenorphine dosing, referral to a more intensive level of ancillary services).
3. If the patient receives a prescription from another physician (e.g., an emergency department), he/she must let the buprenorphine-prescribing physician know promptly.

Rules and Expectations for the Patient

Example items addressed in rules and expectations (continued)

Non-pharmacological treatments

Contacting the physician when the office is closed

Payment of fees

1. An explanation of the role of non-pharmacological treatments should be provided. This can include their importance (that medication rarely addresses all aspects needing treatment in patients with substance abuse), what will be available at the office, what is available in the community, the role of 12 step programs, and when the physician may recommend more intensive levels of non-pharmacological treatments.
2. Procedures for contacting the physician when the office is closed should be provided.
3. An explanation of fees, their payment, and consequences for failure to pay should be addressed.

Rules and Expectations for the Patient

Example items addressed in rules and expectations

(continued)

Cancellation of appointments

Confidentiality

Urine testing procedures

Illicit drug, problematic alcohol use

Arriving at the office intoxicated

1. Some of these points, such as how the office staff will respond to patients who arrive at the office intoxicated, will be discussed in more detail later in this talk.

Rules and Expectations for the Patient

Example items addressed in rules and expectations

(continued)

Loitering

Drug dealing

Aggressive statements/acts

Theft/destruction of property

1. Likewise, several of these topics (such as loitering, drug dealing) will be addressed in more detail later.

Rules and Expectations for the Patient

General principles for rules and expectations

Examples of items addressed in rules and expectations

Conveying rules and expectations

1. While it is important to have rules and expectations, it is equally important that they be communicated clearly and effectively to the patient.

Rules and Expectations for the Patient

Conveying rules and expectations

Do both in writing and verbally

Give the patient a copy

Have patient sign and date a copy, and keep in the patient's chart

Review periodically (as needed) with patients

Review (and revise as needed) periodically with staff

1. The rules and expectations should be conveyed to the patient both in a document form and verbally. The patient should be given the opportunity to ask questions.
2. When reviewing rules and expectations with a new patient, the physician should make it clear that these rules and expectations are reviewed with all new patients being treated with buprenorphine, and that the physician is not bringing them up because he/she is particularly worried about that patient. At the same time, the physician should also convey that these rules and expectations are applicable to all patients equally, and that failure to comply with them will result in consequences.
3. The physician should also discuss with the patients what they can expect from the physician and the physician's office. These expectations can include matters such as being treated in a professional manner, being given notification when the office will be closed, maintenance of confidentiality, and having a means for contacting the physician or a colleague at night and on weekends. Reassurance should be provided to the patient (e.g., that medication will be provided).
4. The patients seeking treatment may be worried about entering treatment (if they are using illicit opioids), or the risks of changing from successful use of a prescription opioid (such as methadone or LAAM). They may be ambivalent about such changes, and worried about being vulnerable to a "new" treatment medication. An opportunity to discuss these matters should be provided to the patient.
5. At the same time the physician reviews the rules and expectations, it also may be useful to give the patient information (in writing) about buprenorphine.

Interactions with the Patient

The initial visit with the patient

Rules and expectations

Boundaries in patient-staff interactions

1. The rules and expectations are an important step in the initial entry of patients into treatment at the office. Boundaries in patient-staff relationships are another aspect of interactions with the patient that should be considered. Maintaining the boundaries is important to the treatment outcome. Treatment staff members have to remain conscious of the therapeutic need to maintain boundaries as patients begin treatment and as the patient-staff relationship evolves during the course of on-going treatment.

Boundaries in Patient-Staff Interactions

Important to consider for the physician, physician's office staff

Maintain professional relationship

Do not accept gifts

Acknowledge away from office only if patient does so

Careful avoidance of excessive familiarity with patients

1. It is important to have discussions with the office staff about the maintenance of boundaries.
2. Avoid allowing patients to become overly familiar. Maintain a professional relationship. Don't use first names with patients and don't allow the patient to call anybody on the staff by his/her first name. If the patient wishes to do so, explain that it is a professional relationship and that maintenance of that professionalism (both by you, and to you) is important.
3. If the patients are encountered away from the office setting (e.g., at a store), respond only if they first acknowledge you. If you are asked who they are (for example, by a family member), simply say they are someone you know from the office. The patients may choose to not acknowledge you to avoid having to explain matters to family (e.g., they say you are their doctor, and a family member then asks for what they are being treated).
4. Do not accept gifts from patients. Do not allow office staff to accept gifts. Accepting a favor from a patient can set up the expectation that a favor will be returned.
5. Avoid discussing your personal matters with patients.

Outline for This Talk

I. Interactions with the patient

III. Urine testing

III. Managing problematic behavior

IV. Summary

1. Drug use is the primary outcome measure in substance abuse treatment, and there are several different mechanisms for measuring drug use. These can include self-reports, reports from other sources of information (e.g., spouse), observation of changes in patient behavior (e.g., cessation of legal problems, drug dealing, stealing; involvement in pro-social activities such as employment or school), and urine testing.

2. Urine testing for drugs of abuse is another aspect of the clinical management of patients with opioid dependence. It is included in this section for several reasons: the policies and procedures you will use need to be explained to the patient at the time of treatment entry (as a part of the rules and expectations); the patient should be told that continued drug use is a problematic behavior and will have consequences; and urine testing can be a highly valuable means for initially detecting drug use (e.g., a relapse to use or initiation of an alternate drug).

[References:

Goldstein A., Brown B.W. Urine testing schedules in methadone maintenance treatment of heroin addiction. *JAMA* 214:311-5, 1970.

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Saxon A.J., Calsyn D.A., Haver V.M., DeLaney C.J. Clinical Evaluation and use of urine screening for drug abuse. *West J Med* 149:296-303, 1988.]

Urine Testing

Why conduct urine drug testing?

Drug abuse a chronic disorder – relapse can occur

Patients may deny or minimize use

Urine testing an integral part of on-going evaluation and treatment planning

1. In order to understand the clinical rationale for urine drug testing, it is important to acknowledge that drug abuse is a chronic disorder and that relapse in drug use can (often does) occur – especially early in the treatment process.
2. Furthermore, patients may deny use – either of illicit opioids, or other drugs. Urine testing provides a means for objectively determining if drug use is occurring.
3. Thus, urine testing should be viewed as both an integral part of the initial evaluation (as a means of confirming opioid use), and as a part of the on-going evaluation and treatment of the patient.

Urine Testing

Different laboratory methods for drug screening and testing

Thin-layer chromatography (TLC):

Inexpensive

Detects high level drug use

1. There are several different laboratory methods that can be used for screening urine samples for drug and alcohol use.
2. TLC is a relatively old technique. It tests the migration of drug on a plate or film (compared to a known control condition).
3. This technique is relatively inexpensive, and allows for the testing of multiple drugs at once. However, it is also somewhat insensitive, and positives on this screening test should be confirmed using another method.

Urine Testing

Different laboratory methods for drug screening and testing (continued)

Gas-liquid chromatography and gas chromatography/mass spectrometry:

Most reliable and most definitive procedure in analytic chemistry for drug detection

Takes days for results

Costs more than other methods

Urine Testing

Different laboratory methods for drug screening and testing (continued)

Enzyme immunoassay (EIA):

Better at detecting drug use (vs. TLC)

Detects presence of drug but not quantity

Common EIA tests: EMIT, FPIA

Can take days for results; cost reasonable

A common EIA drug screen tests for 10 drugs and alcohol

1. EIA techniques are more sensitive than TLC, but not as expensive as GC/MS.
2. Common EIA tests include EMIT (enzyme multiplied immunoassay test), and FPIA (fluorescence polarization immunoassay).
3. These techniques are based on the reaction of the drug with an antibody (with the antibody linked to an enzyme).
4. EIA detects presence of the drug, but not quantity or concentration of the drug in the urine.
5. A common EIA screen is a 10 drug screen plus alcohol. The 10 drugs in the screen are: amphetamine, barbiturate, benzodiazepines, cannabinoids (THC metabolites), cocaine and metabolite (benzoylecgonine), methadone, methaqualone (Quaalude), opiates (morphine, codeine, morphine (heroin metabolite), and hydrocodone), PCP (phencyclidine), and propoxyphene (Darvon).
6. EIA techniques for heroin/morphine have limited sensitivity for detecting synthetic opioids such as oxycodone.
7. Radioimmunoassay (RIA) is similar to EIA, but involves the use of radioactive labeled drug rather than an enzyme linked to the antibody. Drug in the urine (i.e., that isn't radioactive) and the radioactive drug are incubated with antibody. The amount of radioactive drug that doesn't bind to antibody can then be used to determine the amount of drug in the urine.

Urine Testing

Different laboratory methods for drug screening and testing (continued)

On-site testing:

Systems now available that contain reagents in a strip or cup

Allows detection in minutes (indicated by color change)

Cost may be more than immunoassay techniques

1. An example of an on-site testing system is the Abuscreen ONTRAK (which are test strips), and the Syva RapidTest d.a.u. MDN.
2. These are one-step tests that use an immunochromatographic technique.
3. Procedurally, a small amount of urine is applied to a strip (e.g., 3 drops); a color change indicates the presence of the drug for which you're testing.
3. The sensitivity and specificity of these tests is comparable to other immunoassay techniques.
4. Cost may be more than immunoassay techniques.

Urine Testing

Urine detection times for drugs of abuse

Amphetamine/methamphetamine: 2-4 days

Barbiturates: short acting, 2-4 days; long-acting, up to 30 days

Benzodiazepines: up to 30 days

Cocaine: 1-3 days

1. Different drugs and their metabolites remain detectable for different periods of time under different circumstances. There can be considerable variability in the detection times for different drugs.

Urine Testing

Urine detection times for drugs of abuse (continued)

Heroin/morphine: 1-3 days

Marijuana: chronic use, up to 30 days; occasional use,
1-3 days

Methadone: 2-4 days

Phencyclidine: chronic use, up to 30 days; occasional
use, 2-7 days

Urine Testing

Develop plan for testing

Random versus scheduled

If random, how to decide testing schedule

Collection, testing on-site versus off-site

Monitoring of collection

Drugs to routinely test, test to use

1. A frank discussion about urine collection and testing should be held with the patient. It should be pointed out that testing of body fluids (blood, urine) is a routine aspect of the management of a variety of medical disorders (e.g., diabetes, renal disease). Urine testing is a way to monitor treatment progress.
2. Develop a plan for urine testing.
3. Will urine samples be collected on a random basis or scheduled? (Since scheduled testing decreases the likelihood of detecting illicit drug use, random testing is recommended.) One method of implementing a random schedule is to have the patient call the office (for example, each Monday, Wednesday, Friday) to find out if it is a urine collection day.
4. Will collection occur at the office or elsewhere? Is there somewhere else, perhaps near the patient's home, where a urine sample can be collected and tested?
5. How will the collection of the sample be monitored (both for on-site and off-site collecting)? Direct observation of the collection should be done by a same sex staff member. Have the patient leave coats, bags, purses etc., outside the bathroom. If not observed, consider checking the temperature of the sample. (Collection cups with built-in temperature strips are available.) If tampered samples are suspected and observed collection is not possible, use another method of verifying the sample.
6. Testing can now be done on-site, using test strips or cups that contain detection elements that change in the presence of a specific drug.
7. For what drugs will you test? Test for the drugs which the patient may be using. Consider opioids (morphine), cocaine, methadone, benzodiazepines, cannabis.

Urine Testing

Develop plan for responding to a positive result

Consider stage of treatment

Consider class of drug found in urine

Consider range of consequences (pharmacological, non-pharmacological)

1. In addition to developing a plan for urine testing, there should also be a plan for responding to a positive test result.
2. The response can vary depending upon the circumstances of the patient. An opioid positive result early in treatment suggests that the patient may need a higher dose of buprenorphine. A positive test result later in treatment for a non-opioid drug (e.g., cocaine) suggests a referral for more intensive non-pharmacological services (e.g., treatment at a partial hospitalization program), to help the patient reach the goal of abstinence from all drugs of abuse.
3. In addition, the positive result should be assessed in the context of the patient's recent behavior. Results positive for opioids in the context of loitering and lost prescriptions suggest evaluating the patient for possible diversion of medication.
4. A positive test result for an otherwise stable patient at a time of life changes or increased stress suggests a referral for counseling or therapy.

Outline for This Talk

- I. Interactions with the patient
- II. Urine testing
- III. Managing problematic behavior**
- IV. Summary

1. The third section of this talk will now turn to a discussion of the management of problematic behaviors. Again, it is worth repeating that it is probable that such difficulties will be quite rare – but it is in the best interest of the physician, the office staff and the patient to be prepared for such possibilities.

2. It is important to anticipate such events and have well-thought through procedures adapted to the clinician's particular practice situation. Procedures may vary somewhat depending upon the structure of the office practice (e.g., solo versus group practice with a shared waiting room; the availability of methadone programs and ancillary drug treatment resources).

Problematic Behavior

General principles in response to problematic behaviors

Specific problematic behaviors

1. We will begin with some general points about the management of problematic behaviors and then discuss in more detail specific behaviors. These general points can be applied to all the problematic behaviors reviewed.

General Principles

Consider history of patient's treatment success, patient's motivation, options available

Be aware of impact on staff and other patients if it is perceived that there is no consequence to the patient

1. First, it is useful to consider the patient's history when evaluating a problem. People early in treatment may have some problems – a relapse in drug use – that can be viewed as a part of the natural stabilization process of treatment. If they are motivated, then the physician may choose to continue working with them. Alternately, a patient who has an early relapse and is found to be repeatedly selling prescriptions to finance other drug use is probably not a good candidate for continued office-based treatment.
2. If there are no consequences to patients who show problematic behaviors, this can be disruptive to staff, to other patients in treatment, and to the local community.

General Principles

Consider a range of options in response to problematic behaviors. Consider:

Increased office visits

Referral to more intensive level of service such as counseling

Change in dosing schedule

Discharge to methadone or LAAM treatment

1. There are a variety of options available to the physician. They should be considered in the order of their intensity. The response by the physician should be tailored to the severity of the problem and the stage in treatment of the patient.

General Principles

Negotiating skills and problematic behaviors

Negotiate from strength:

Keep in mind you control things the patient wants (a reinforcing medication that prevents withdrawal, a less restrictive and stigmatizing setting in which to receive the medication)

1. When discussing (or confronting) patients about their problematic behaviors, it is useful to keep in mind several points. Negotiating skills can help the clinician to successfully manage the situation.
2. First, keep in mind that you control things that the patient desires – that you are in a position of strength. These things that you control include things such as the medication, the frequency the patient needs to see you to get prescriptions for the medication, and the setting at which treatment is delivered.

General Principles

Negotiating skills and problematic behaviors (continued)

Defend the integrity of treatment:

Goals of treatment

Safety of treatment for the patient

Safety and comfort for you, your staff, other patients

Safety of the community

1. When meeting with the patient about problematic behaviors that have been identified, it can be useful to stress to the patient the need to defend the integrity of treatment. Explain that you must defend the goals of treatment, the safety of treatment for the patient, and the safety and comfort of you, your staff, and other patients. Jeopardizing treatment impacts not just the patient who may be transferred out of your care, but the treatment of other patients.

General Principles

Negotiating skills and problematic behaviors (continued)

Consider violations in the context of the patient's condition:

Do not excuse or ignore violations

See violation as an indication for a higher level of care

1. Breaking rules of treatment should not be ignored. They should be evaluated in the context of the patient's condition. For example, a violation by a patient who is doing well in other areas and complying with other rules may be seen differently from a violation by a patient who is making no progress toward treatment goals and/or who is violating other rules.
2. Violations should be seen as an indication that more intensive levels of treatment are needed.

General Principles

Negotiating skills and problematic behaviors (continued)

Be aware of your feelings:

Look for anger, guilt, disappointment

Trapped, helpless, or manipulated

1. Finally, be aware of your own response to patients who have demonstrated problematic behaviors. You may feel personally hurt by their behavior, or angry, guilty, and disappointed. You may also feel trapped by the situation (although you should keep in mind that you are in control of treatment).

Problematic Behavior

General principles in response to problematic behaviors

Specific problematic behaviors

1. We will now review specific problematic behaviors.

Specific Problematic Behaviors

Intoxication at the office

Loitering

Diversion of medication

Drug dealing

Aggressive acts

Stealing from the office

1. In this section we'll review six different problematic behaviors that might occur with opioid dependent patients.
2. Again, it should be stressed that the likelihood these behaviors will occur for most patients is quite small. The overwhelming majority of patients with opioid dependence who seek treatment are cooperative and wish to move on with their lives and stop using drugs. They do not enter treatment intending to deal drugs, loiter, or vandalize. Such actions occur rarely – but when (if) they do occur, it is important that the office be prepared to respond in a therapeutically appropriate and consistent way.
3. This first portion addresses the patient who arrives at the office with evidence of intoxication. A related situation is the patient who arrives at the pharmacy with evidence of intoxication. The general procedures outlined here for intoxication at the office can also be applied to management of the patient who arrives at a pharmacy intoxicated.

Problematic Behavior

Intoxication at the office: Alcohol

Consider having a breath analyzer available on site

Determine how the patient got to the office, and how the patient will get home

Address alcohol use with patient – better to wait until sober

Arrange for treatment

1. Hand-held breath analyzers are available and relatively inexpensive.
2. If the patient is intoxicated with alcohol, then it is important not to allow him/her to drive after seeing them in the office.
3. Confronting patients about their alcohol use is best done when they are not under the acute influence of alcohol. Wonderful interventions made with an intoxicated patient are often forgotten by the patient when they are sober.
4. Arrange for the patient to have his/her alcohol use addressed. Do not treat alcohol use with naltrexone (ReVia) because you risk precipitating withdrawal with this opioid antagonist.

Problematic Behavior

Intoxication at the office: Illicit drugs

Assess for type of drug used; may be useful to have on-site urine test available

Approach follows a similar logic as described for alcohol: determine how the patient got to the office and how the patient will get home, address use with patient (but better to wait until not intoxicated), arrange for treatment

1. A patient may come to the office under the influence of drugs other than opioids or alcohol.
2. The approach to evaluation of the patient should follow a similar logic as that for the patient who presents intoxicated with alcohol.
3. A special caution should be noted if intoxication with benzodiazepines is suspected, since there have been reports from France of deaths associated with the combination of buprenorphine and benzodiazepines. (This is discussed in more detail in another section.)

Problematic Behavior

Intoxication at the office

Loitering

Diversion of medication

Drug dealing

Aggressive acts

Stealing from the office

Problematic Behavior

Loitering

Assess patient's use of time

Consider if patient is dealing drugs

Explore options to structure time

Recognize some patients seek the comfort of a safe place

1. Loitering may be due to drug dealing – a pattern of loitering and lost prescriptions should raise suspicion of drug dealing.
2. Loitering may also be due to unstructured time, and the patient's desire to remain at a safe place (and not go home, where drug use may be occurring).
3. Consider referring the patient to a psychosocial or vocational rehabilitation treatment program, if they seem to have unstructured time on their hand.

Problematic Behavior

Intoxication at the office

Loitering

Diversion of medication

Drug dealing

Aggressive acts

Stealing from the office

1. Another potential problem is that a patient on buprenorphine diverts or sells their medication and/or prescription.

Problematic Behavior

Diversion of medication

Direct evidence of diversion (e.g., caught by police)

Indirect evidence of diversion (repeated losing of prescriptions)

Options can include transfer to more intensive level of treatment (e.g., methadone clinic); initiate psychosocial services (e.g., counseling, group therapy); more frequent monitoring at office (e.g., weekly visits); alternate buprenorphine dosing schedule (e.g., 3x/week)

1. You may become aware of diversion through direct evidence or indirect evidence.
2. Patients for whom there is direct evidence that they are diverting buprenorphine should lose the opportunity to receive office-based buprenorphine treatment. These patients should be transferred to methadone treatment. Such actions seriously jeopardize buprenorphine treatment for patients who are compliant with treatment.
3. If a patient reports losing a buprenorphine prescription, consider assessing for needle marks. The patient might be misusing the buprenorphine – for example, dissolving and injecting some of the buprenorphine tablets (with the resultant better bioavailability), and then selling the others.
4. Patients for whom there is indirect evidence that they are diverting buprenorphine can be managed in several different ways. They, too, can be transferred to methadone treatment. Alternately, they can be required to attend the office more frequently for their medication. If they are on a daily schedule, it may be possible to switch them to thrice or twice weekly dosing, and have them come and take all doses at the office (i.e., no prescription and no take-home doses).

Problematic Behavior

Intoxication at the office

Loitering

Diversion of medication

Drug dealing

Aggressive acts

Stealing from the office

Problematic Behavior

Drug dealing

May be reported by staff, security personnel as suspicious behavior noted in vicinity

Dealing could be of other drugs (not buprenorphine)

Consider impact on community

1. Evidence of drug dealing may be direct (e.g., an arrest by the police, witness of dealing by staff), or indirect (e.g., losing of prescriptions, reports by other patients that they have been approached and offered drugs by someone in treatment with the physician).
2. If there is direct evidence of drug dealing, then discharge from office-based treatment should be strongly considered. (The rules and expectations can lay out this consequence to patients.) Drug dealing undermines office-based treatment for opioid dependent patients, and risks that buprenorphine will only be available through special clinics (e.g., methadone clinics).
3. Indirect evidence of drug dealing should be addressed with the patient. The discussion should be matter-of-fact and should remind the patient of the consequences if there is direct evidence of drug dealing.
4. Drug dealing in the waiting room is unacceptable and should result in discharge to a more intensive and structured level of service.

Problematic Behavior

Intoxication at the office

Loitering

Diversion of medication

Drug dealing

Aggressive acts

Stealing from the office

1. The next problematic behavior reviewed here is aggressive acts.

Problematic Behavior

Aggressive acts

Examples: vandalism, threatening staff, other patients

Clearly convey at time of treatment entry such acts unacceptable

Decide consequence (e.g., terminate treatment, referral to a clinic), follow through

1. In the rules and expectations discussed with all patients, it is good to include a section on aggressive acts and consequences.
2. If a patient threatens a staff member, then treatment at the office should be terminated. Notification of the police may be indicated (as discussed in the lecture on confidentiality), and support for the staff member should be provided (e.g., escorts to his/her car).
3. A patient could threaten another patient – for example, someone he/she knew from the time of active drug use. If the threat is significant – that is, it has a high level of intent (i.e., not simply a casual statement that on probing has an extremely low level of intent), then discharge from office-based treatment should be entertained. If the patient has otherwise done well in office-based treatment, then possible transfer to another office could be considered. A duty to warn the threatened patient should also be considered. If the intent is low, then scheduling of patients and/or patient flow may be arranged to minimize the overlap of appointments for buprenorphine maintained patients.

Problematic Behavior

Aggressive acts (continued)

If act occurred at another time (e.g., vandalism), have evidence available

If no evidence, consider source of information, severity of act, and patient's treatment history

Closer monitoring may be appropriate

Consider possible etiologies (e.g., acute mania, delirium, psychosis)

1. Vandalism can be difficult to address – in part because such acts may be suspected but not witnessed.
2. If witnessed (e.g., by a staff member), then this needs to be discussed with the patient. The consequences should be appropriate to the level of vandalism, and may also take into account the patient's overall level of success in treatment. The patient, for example, may be required to pay for fixing the problem created (e.g., damage), and more closely monitored on days of appointments.
3. If not witnessed but suspected, then closer scrutiny of the patient (e.g., as they leave the office) may be warranted.
4. Keep in mind that patients who are manic, delirious, or psychotic may have aggression related to an acute episode of one of these illnesses. Treatment of the underlying condition is the first and necessary step in stabilizing and managing the patient.

Problematic Behavior

Aggressive acts (continued)

If need to confront agitated patient acutely:

Determine if they have a weapon; call police

Do so with others

Be calm, maintain professionalism

Move patient away from other patients (or move other patients)

Do not physically contact patient

1. If a patient is at the office and is agitated, keep the following points in mind.
 - a. First, if the patient has a weapon (gun, knife), don't attempt to confront the patient. Call the police.
 - b. If you are confronting the patient, do so with others. Select a person who will talk with the patient, but don't do so one-on-one. Convey to the patient that he or she is dealing with a group, and is outnumbered.
 - c. Be calm, maintain professionalism. Appeal to a history with the patient ("we've been working well together, this isn't the way you act").
 - d. Move the patient away from others, or move other patients away from the agitated patient.
 - e. Do not move close to the patient. Maintain a safe distance until they have calmed. If you have to be close to them, remove articles of your clothes that can be grabbed and pulled (ties, scarves, ID badges on chains).
 - f. You don't have to deal with the problem. You can call the police. Don't try to be a hero.

Problematic Behavior

Intoxication at the office

Loitering

Diversion of medication

Drug dealing

Aggressive acts

Stealing from the office

1. Finally, the last problematic behavior reviewed here is stealing from the office.

Problematic Behavior

Stealing from the office

Patients may steal needles, syringes, prescription pads, purses or more major items such as equipment from the office (e.g., exam room)

Keep items secure

Don't leave patient unattended

Address stealing with consequences

1.

Outline for This Talk

- I. Interactions with the patient
- II. Urine testing
- III. Managing problematic behavior
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Summary

Most patients treated in an office-based setting will be cooperative, stable

Having rules and regulations helps patients and office staff prepare responses to problematic acts

The physician should have options in how to respond – not every response should be discharge from treatment

Patient Confidentiality

Patient Confidentiality

The purpose of this section is to review issues associated with confidentiality for patients receiving substance abuse treatment. There are specific Federal regulations for the confidentiality of substance abuse treatment, and states may have further such regulations. It is important for the clinician providing office-based buprenorphine treatment to be familiar with these regulations, as they may apply to his/her practice and treatment of patients with substance abuse disorders.

- 1.

Outline for This Talk

- I. Introduction
- II. Purpose
- III. Scope of the law
- IV. General rules
- V. Exceptions
- VI. Summary

1. A good reference for issues of confidentiality and disclosure is the Technical Assistance Publication (or TAP) #13, published by CSAT. It is titled “Confidentiality of Patient Records for Alcohol and Other Drug Treatment.”
2. This publication is free (along with other TIPs and TAPs), and can be ordered from the National Clearinghouse for Alcohol and Drug Information (1-800-729-6686 or 1-301-468-2600).

[References:

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Outline for This Talk

- I. Introduction
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1. We will begin with a brief introduction to issues of patient confidentiality.
2. It is important to note that we're going to review federal laws (in place at the end of the year 2000) associated with confidentiality and disclosure. However, there can also be state laws and regulations governing confidentiality.
2. This is a topic that can change (both at the federal and state levels). Thus, material covered here may be out of date in a few months, or need further elaboration depending upon local (i.e., state) laws and regulations.

Introduction

Genesis in two statutes of the early 1970s

Implemented by regulations from HEW in 1975

Revised by HHS in 1987 (42 CFR Part 2)

Congress reaffirmed and reorganized the two statutes into a single act

1. Two statutes in early 1970s: Comprehensive Alcohol Abuse and Alcoholism Prevention, Treatment and Rehabilitation Act of 1970; and the Drug Abuse Prevention, Treatment and Rehabilitation Act of 1972. These statutes were then implemented through regulations released by the Department of Health, Education, and Welfare (HEW) in 1975.
2. The Department of Health and Human Services (HHS) revised the 1975 regulations in 1987 (title 42, part 2 of the Code of Federal Regulations).
3. Congress merged the two acts by combining the original statutes into one act (the Public Health Service Act; title 42, section 290dd-3 of the United States Code). The merger did not affect the confidentiality regulations.

Outline for This Talk

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1. Next we will briefly review the purpose for these confidentiality laws and regulations.

Purpose

People with substance abuse problems are more likely to seek and succeed at treatment if they know their need for treatment will not be disclosed unnecessarily

Regulations restrict both disclosure and use of information about individuals in federally assisted drug and alcohol treatment programs

1. The regulations apply to any federally assisted drug and alcohol treatment program (and this can include individual practitioners). Such programs and practitioners that are federally assisted include those:

- operated by the federal government
- certified for Medicaid reimbursement
- receiving federal block grant funds (through local government)
- licensed by the federal government
- exempt from paying taxes

2. This coverage is so broad that for all practical purposes any treatment program is covered and many individual practitioners may be covered (e.g., if receiving Medicaid reimbursement). Anyone providing substance abuse treatment, regardless of setting, should be familiar with these protections and how to comply with them.

Outline for This Talk

- I. Introduction
- II. Purpose
- III. **Scope of the law**
- IV. General rules
- V. Exceptions
- VI. Summary

1. Now we will talk about the scope of the law.

Scope of the Law

Overview

Application

Strictness of regulations

Consequences of violating or disregarding

Conflicts with state laws

1. In this section, we will review these five topics regarding the scope of the confidentiality laws. We'll begin with an overview.

Scope of the Law

Overview

Restricts disclosure and use of patient-identifying information

Patient-identifying information is anything that reveals a person is receiving, has received, or has applied for substance abuse treatment

Can't disclose participation in substance abuse treatment – but can disclose identity under some circumstances

1. Care must be taken to assure that information is not inadvertently given out. Thus, for example, a receptionist who has identified a program by name should not then reveal information that indicates the person is a patient in the program (either directly or indirectly).
2. However, there are circumstances whereby the person can be identified (besides giving consent, which will be reviewed later). For example, if the treatment program is part of a hospital, then confirmation that the person has been in treatment at the hospital can be made (for example, without specifying that their treatment was for substance abuse treatment).

Scope of the Law

Overview

Application

Strictness of regulations

Consequences of violating or disregarding

Conflicts with state laws

Scope of the Law

Application

Regulations apply to holders, recipients, and seekers of patient-identifying information

Individual/program can't release information except as authorized by the patient or as permitted by regulations

Scope of the Law

Application (continued)

Anyone who receives information can't re-disclose without patient consent or as authorized by regulations, and may not use it except for certain purposes

Anyone seeking information can't compel its disclosure except as permitted by regulations

Scope of the Law

Overview

Application

Strictness of regulations

Consequences of violating or disregarding

Conflicts with state laws

Scope of the Law

Strictness of Regulations

Federal confidentiality regulations more strict than most other confidentiality rules

They apply whether the person seeking the information already has it; is seeking it for judicial or administrative proceedings; is a law enforcement or other government official; has a subpoena or a search warrant; is the spouse, parent, relative, employer, or friend

1. Someone could already have the information in one role (e.g., as one program's part-time physician), and want it in a second role (e.g., as a second program's physician). The regulations apply in such a situation.

Scope of the Law

Overview

Application

Strictness of regulations

Consequences of violating or disregarding

Conflicts with state laws

Scope of the Law

Consequences of Violating or Disregarding

Criminal penalty

For a program, could lose license or certification

Patients may sue

1. The criminal penalty can be in the form of a fine of up to \$500 for the first offense, and up to \$5000 for each subsequent offense.

Scope of the Law

Overview

Application

Strictness of regulations

Consequences of violating or disregarding

Conflicts with state laws

Scope of the Law

Conflicts with State Laws

State laws or regulations can be more restrictive than federal regulations, but they can't reduce the restrictions contained in federal regulations

1. Some exceptions to federal regulations are possible, as will be reviewed later. For example, patient disclosure can occur under certain circumstances (e.g., crimes against personnel of a treatment program or office). State laws or regulations could be written to incorporate such exceptions. However, the state law cannot create more exceptions than those found in the federal regulations.

Outline for This Talk

- I. Introduction
- II. Purpose
- III. Scope of the law
- IV. General rules**
- V. Exceptions
- VI. Summary

General Rules

Programs and individual practitioners

Disclosure

Patient

1. Next we will review some general rules and definitions regarding confidentiality and substance abuse treatment. These rules will be examined as they pertain to programs and individual practitioners, disclosure of information, and the patient.

General Rules

Programs

Definition of a program: federally assisted organizations and individual practitioners (MDs, psychologists, others)

1. A “program” is defined as either an organization or an individual practitioner. For purposes of these regulations, an individual physician in an office setting can be considered a program. (For the sake of clarity, this section includes the term “individual practitioner” when referring to programs, although this is actually redundant with respect to the Federal regulations.)

General Rules

Programs (continued)

Federal assistance:

- Operated by the Federal government
- Certified for Medicaid reimbursement
- Receiving Federal block grant funds
- Licensed by the Federal government
- Exempt from paying taxes

1. A program or individual practitioner qualifies as being federally assisted if any one of the five above criteria are met.

General Rules

Programs (continued)

What programs (including individual practitioners) do:
specialize in providing, in whole or in part,
individualized alcohol or drug abuse diagnosis,
treatment, or referral for treatment

1. These regulations apply to a a program or individual practitioner if the program or individual practitioner does the above.

General Rules

Programs (continued)

Location of programs (and individual practitioners): free standing, part of a larger organization (in a hospital, part of a larger clinic)

Staff in the program: part- and full-time employees; volunteers; student interns; former staff; executive, administrative, clinical and support staff

General Rules

Programs and individual practitioners

Disclosure

Patient

General Rules

Disclosure

Communication that directly or indirectly identifies someone as being, having been in, or having applied for substance abuse treatment

Occurs when a program or practitioner discloses: patient's record; allows an employee to testify about a patient's treatment; allows a receptionist to confirm a person is a patient in the program; uses identifying stationery; discloses anecdotal information

General Rules

Programs and individual practitioners

Disclosure

Patient

General Rules

Patient

Anyone who has applied for or received a diagnostic examination or interview, treatment, or referral for treatment at a drug or alcohol program

Applicants for services are covered even if they fail to show for their initial appointment, or elect to not follow up with treatment

Includes current, former, and deceased patients

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Exceptions

Internal communications

Consent

Anonymous or non-patient identifying information

Qualified service organization agreement

Crimes on premises or against personnel

1. There are several possible exceptions to the confidentiality regulations, as listed on this and the next slide. We're going to go through each of these in turn. There are five additional exceptions listed on the next slide.

Exceptions

Medical emergencies

Mandated reports

Research

Audit and evaluation

Court orders

Exceptions

Internal Communications

Can occur within a program/office or with an entity having direct administrative control, if information is needed

Staff can share information with each other, supervisors

Staff of the hospital's record-keeping or billing department

1. Staff of a program or office can share information amongst themselves. They can also share information with administrative supervisors who have direct oversight of the program or office.

Exceptions

Consent

Patient can authorize specific disclosures

The patient's consent must be in writing

Consent must contain: name of patient; name of disclosing program; purpose of disclosure; who is to receive; exact information to be released; that patient understands he/she can revoke consent at any time; revocation can be oral; date/condition under which consent expires; date signed; patient's signature

1. The patient can revoke the consent at any time, and can do so orally as well as in writing. The consent form should also inform the patient that revocation is possible only to the extent that action has not been taken on the release of information.
2. Further information on consents is provided in the Medical Record Keeping section.

Exceptions

Consent (continued)

Program (or office) has to receive a copy of the patient's consent before responding to request

Disclosures must include a written notice prohibiting re-disclosure

The re-disclosure prohibition must be sent to recipient even when disclosure is made orally

Exceptions

Anonymous or Non-patient Identifying Information

Disclosure may reveal a patient's name, address, telephone number without violating regulations when it does not reveal the nature of the services received by the patient or provided by the program

1. Thus, for example, a program or office could report to a local health board that a patient has tested positive for tuberculosis (a positive PPD test), without needing to obtain the consent of the patient – assuming the program or office conveys the information without revealing the patient is in substance abuse treatment.

Exceptions

Qualified Service Organization Agreement

Program or office can disclose to QSO without consent

QSO: a person or agency that provides services that the program/office itself does not provide (e.g., data processing, dosage preparation, vocational counseling)

QSO must be qualified to communicate with the program/office (i.e., written agreement)

1. Other services that may be provided by a QSO are: laboratory analyses and professional services (legal, medical, accounting).
2. The written agreement with the QSO must: a) acknowledge that the QSO is bound by the federal confidentiality regulations; b) promise not to re-disclose patient identifying information to which it becomes privy; c) promise to resist unauthorized efforts to gain access to any patient identifying information that may come into its possession.

Exceptions

Qualified Service Organization Agreement (continued)

Program or office may freely communicate with QSO
only the information needed by QSO

Program or office can enter into such an agreement only
if QSO offers service the program/office does not offer

Program/office doesn't have to inform patients about
QSOs

Exceptions

Crimes on Premises or Against Personnel

Regulations permit a program or office to release patient identifying information to the police if a patient commits or threatens to commit a crime on the premises or against program/office staff

Can give name, address, last known location

Can't report patient's other crimes

Exceptions

Medical Emergencies

Medical emergency: situation posing immediate threat to health of the patient and requiring immediate medical intervention

Information can be released to medical personnel who need to treat the condition

This exception cannot be used to release information to family or non-medical personnel

1. For example, the program or practitioner could release information to an emergency department physician or nurse who is treating a patient following a significant motor vehicle accident.
2. However, the program or practitioner cannot release information to family members who, for example, state they are calling from an emergency department and need to know if their family member is in treatment at the program.

Exceptions

Mandated Reports

States require reporting of cases of child abuse or neglect (to child welfare authorities)

Can report such cases to the state (including in writing), but regulations continue to apply regarding patient's records

1. Reporting suspected child abuse cases to the state needs to occur. However, information about the fact that the patient is receiving treatment in a substance abuse program or from an individual practitioner should remain confidential.

Exceptions

Research

Program or individual practitioner may allow a researcher to have access to patient records

Program director/ individual practitioner must verify researcher qualified, protocol protects records, patient identification will not be re-disclosed

Research protocol needs outside review

1. Programs and individual practitioners do not have to allow a researcher access to their records. However, programs/practitioners may wish to cooperate because research is helpful in moving the field of substance abuse treatment forward, and can give clinic and office staff the opportunity to participate in timely topics.

2. If the program/practitioner decides to allow access to patient records, then outside review must be done by three or more independent evaluators who determine that rights and welfare of patients are protected and that the benefits of the project outweigh the risks.

Exceptions

Audit and Evaluation

May be conducted by regulatory agencies; funders;
private third-party payers; private peer review
organizations

Time-limited activity for audit or evaluation

Can't re-disclose information except pursuant to a court
order or to determine Medicaid/Medicare compliance

1. Audits and evaluations can have access to patient information, but they must be time limited – they can't be used to gain access to records on an on-going basis.

Exceptions

Court Orders

A federal, state, or local court may authorize a program or individual practitioner to make a disclosure of confidential patient identifying information only after following certain procedures and making certain determinations

A subpoena, search warrant, or arrest warrant is not sufficient by itself to require or permit disclosure, even if signed by a judge

Exceptions

Court Orders (continued)

Procedure to get a court order:

Program/practitioner and patient must be given notice of application for the order and opportunity to respond (unless information is to investigate or prosecute the patient, then patient is not entitled to notification; if program/ practitioner is target of investigation, then it, too, is not entitled to notification)

Exceptions

Court Orders (continued)

The application and any court order must use a fictitious name for the patient

All court proceedings must remain confidential unless the patient requests otherwise

The court must find “good cause” before it orders the disclosure

Exceptions

Court Orders (continued)

Good cause: must be in the public's best interest; need for disclosure must outweigh the adverse effect (on patient, doctor-patient relationship, and effectiveness of program/practitioner services); the information must not be available from any other source. The judge is entitled to examine records before making a decision

Exceptions

Court Orders (continued)

There are limits, even with “good cause” – must be limited to essential information; dissemination of information limited to those who need to know; court should take steps to protect patient’s confidentiality

1. Protection of patient’s confidentiality may occur, for example, by sealing the records of the proceedings.

Exceptions

Court Orders (continued)

If information sought is a “confidential communication” then it may not be disclosed unless disclosure is necessary to protect against threat to life/serious bodily harm; is necessary to investigate or prosecute an extremely serious crime; or is connected with a proceeding in which the patient has already presented evidence concerning the confidential communication

1. Thus, even a court order cannot force the release of confidential communications made to the program or practitioner unless one of these three situations is fulfilled.

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1. This completes our review of confidentiality and disclosure. Some final notes are worth emphasizing:

- a) These issues of confidentiality and disclosure can be quite complicated. The practitioner or program should strongly consider engaging the services of a lawyer familiar with this area, if the practitioner or program has an issue arise in one of these areas.
- b) Office procedures should comply with these requirements.
- c) Every staff member should be informed of how rigorously the government protects the patient's identity and how serious the consequences might be if there is an inadvertent disclosure (e.g., fine, loss of license).

2. With this caveat in mind, it is useful to find out before hand what lawyer(s) in the local community are familiar with these confidentiality regulations. This will allow you to be prepared in the case that a confidentiality issue comes up.

Summary

Confidentiality of substance abuse treatment is more stringent than typical regulations for doctor-patient relationship

Disclosure of information requires special consent of patient; other circumstances may allow disclosure

Be familiar with regulations for confidentiality, and be prepared for requests of records

Office Policies & Procedures

Office Policies and Procedures

The purpose of this talk is to review aspects of office management that are related to the treatment of opioid dependent patients with buprenorphine. There is overlap between this talk and several others, such as the talks on confidentiality and clinical management, and all of these topics should be considered in the set-up and operation of office-based treatment with buprenorphine.

Clinicians who already operate an outpatient practice may wonder why it is necessary to have a section on office management. There are several day-to-day operational aspects of office-based buprenorphine treatment that significantly differ from the routine practice of medicine. This section addresses these topics, in order to better prepare the clinician to successfully treat opioid-dependent patients with buprenorphine.

1. Changes in office practice can be categorized by whether they are made to accommodate the needs of specific patients (e.g., a change in office hours to allow appointments for patients who are working), and changes that are necessary for maintaining the clinician's comfort in treating patients with opioid dependence. When considering this latter point, the clinician may include considerations such as the safety and well being of other patients and staff, and the desire to maintain buprenorphine as a viable treatment option for the office.

The distinction between changes made for the patient and changes made for the physician and staff is of more than academic importance. When there is conflict, the patients tend to argue benefits from their point of view. As the treating physician, you have to attend to the patient needs as well as yours and your staff's. Overall, your decisions must be designed to sustain an office capable of maintaining a therapeutic milieu that fosters recovery from opioid dependence. Your needs and your staff's needs deserve consideration. If these needs are not considered, the enterprise of office-based buprenorphine treatment runs an increased risk of failure.

Outline for This Talk

- I. Necessary resources
- II. Working with office staff
- III. Information for the patient
- IV. Financial issues
- V. Community relations
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Outline for This Talk

- I. Necessary resources
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1. We will begin with a discussion about the resources that should be in place before starting office-based buprenorphine treatment.

Necessary Resources

When preparing for office-based buprenorphine treatment, arrange to have the necessary resources in place.

These include:

Referral resources

Capacity to get valid urine test results

Coverage

Medication security and storage

1. There are four types of resources that should be arranged, and we'll briefly consider each of these in turn starting with referral resources.

Necessary Resources

Referral resources

Different levels of substance abuse treatment services

Psychiatric or medical services

Other community resources (e.g., AA, NA)

1. The physician should be aware of the different types of substance abuse treatment available in the local community. Specifically, services such as methadone and LAAM, partial hospitalization, intensive outpatient, and group counseling programs should be identified. Procedures for admitting patients to these different services should be obtained. Further discussion of several of these services is provided in the section on Non-pharmacological Treatments.
2. The psychiatrist should identify an internist or family physician for referral of medical problems (such as hepatitis C treatment). If the psychiatrist does not do physical examinations, then he/she will need to arrange to have someone available to do them (and that person should have familiarity with the common co-morbid medical problems found in substance abusing patients). Similarly, the internist or family physician should identify a psychiatrist who will accept referral of patients (e.g., for treatment of major depression or severe personality disorders).
3. Other community-based services, such as self-help groups and 12 step programs, should also be identified.

Necessary Resources

Capacity to get valid urine test results

Collection procedures in office or off-site

Shipment for testing

Testing site

1. The physician should set up a mechanism for urine testing. Considerations should include:

- a) on-site versus off-site collection and testing
- b) procedures for collecting urine if it is to be on-site
- c) assurance that off-site collection is a valid collection
- d) shipping of samples if collected on-site
- e) the turn-around time for testing done off-site
- f) the methods and validity of the off-site testing procedures

Necessary Resources

Coverage

Be realistic – 24 hour coverage, 7 days per week is not sustainable

Covering physician with knowledge and experience using buprenorphine, the office policies and procedures

1. Finally, a necessary resource is coverage for when the physician is unavailable.
2. The covering physician should have experience in taking care of opioid dependent patients, and ideally should have experience prescribing buprenorphine. Physicians who lack this experience may fail to provide necessary care to patients, and may have the patient take advantage of their inexperience.

Necessary Resources

Medication security and storage

Governed by Drug Enforcement Agency (DEA)

Requirements regarding buprenorphine kept in an office
not yet known

Probable that limited amounts will be allowed on-site
(with filling of prescriptions at a pharmacy)

1. Currently (January, 2001), regulation governing medication security for methadone and LAAM comes from the DEA. These DEA regulations (Parts 1301-1307) can be found in Appendix C of TIP 1 (State Methadone Treatment Guidelines). This publication is free (along with other TIPs and TAPs), and can be ordered from the National Clearinghouse for Alcohol and Drug Information (1-800-729-6686 or 1-301-468-2600).
2. The regulations governing buprenorphine security are not known at the present time.
3. These current regulations for methadone and LAAM include stipulations about the storage of controlled substances (e.g., locking of a safe or cabinet).
4. It is expected that buprenorphine (and buprenorphine/naloxone) will be scheduled. It is also expected that provision will be made to allow physicians to maintain a supply of buprenorphine and buprenorphine/naloxone in their office, so that patients can be started promptly on medication, if needed. But it is not known if there will be regulations governing its storage in the office setting.

[Reference:

Parrino M.W. (ed) State Methadone Treatment Guidelines. Technical Improvement Protocol #1, U.S. Department of Health and Human Services, Center for Substance Abuse Treatment, Rockville, Maryland, 1993.]

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1. Next, we will turn to a discussion about working with office staff as you set up office-based treatment of opioid dependence with buprenorphine.

Working with Office Staff

Staff education

Training personnel to provide quality care

Universal precautions

1. Before beginning treatment with buprenorphine in the office, staff education should be conducted.

Working with Office Staff

Staff education

Treating patients with substance abuse disorders

The disorder of opioid dependence

Role and importance of medication in treatment of opioid dependence

1. It is useful to begin by making some general points about the treatment of patients with substance abuse disorders. The treatment of patients who have a substance abuse disorder does differ from the treatment of many other conditions typically seen in office-based practice. (While it is popular to try to equate drug abuse with other medical conditions, other medical disorders do not typically involve, for example, a pattern of repeated violation of laws and social norms.) Staff should have a positive, non-judgmental and therapeutic attitude toward patients with opioid dependence. At the same time, office procedures and patient interactions should be designed to minimize the chance for patients to steal or deceive the physician and staff.
2. A general introduction to the disorder of opioid dependence should be provided to the staff. How the diagnosis is made, the extent of opioid dependence, and other topics taken from these talks and the Buprenorphine Guidelines can be presented (depending upon the familiarity of the office staff with substance abuse disorders and opioid dependence treatment).
3. The role of medication in the treatment of opioid dependence should be discussed. The extent of methadone treatment, its efficacy and safety, and the linkage of methadone medication with non-pharmacological treatments should be reviewed. Well-run methadone programs can be highly effective in the treatment of opioid dependence. It is likely that some stable patients from methadone treatment programs will want to transfer to office-based buprenorphine treatment. This should be explained to staff – that there are many patients in methadone treatment who should have a smooth transition to buprenorphine, and then require monthly office visits with minimal other management required.

Working with Office Staff

Staff education (continued)

- Maintenance of patient confidentiality
- Treatment philosophy
- Providing medication
- Role of non-pharmacological treatments

1. Rules and regulations regarding patient confidentiality (as reviewed in a separate talk on Clinical Management) should be discussed in detail and stressed with staff.
2. The treatment philosophy which will guide your work with patients should be discussed thoroughly with staff. The treatment philosophy, which is also reviewed in the talk on clinical management of the patient, can include points such as:
 - a) The physician's belief about the nature of substance abuse
 - b) The goal(s) of treatment
 - c) The proper approach to treating patients
3. The providing of medication should be reviewed with staff. This includes the procedures for the storage and administration of buprenorphine at the office (i.e., during the induction phase), as well as the management of lost prescriptions for patients who are in the maintenance phase of treatment.
4. The physician should review with staff how on-site non-pharmacological treatment will be provided and what services off-site will be utilized.

Working with Office Staff

Staff education

Training personnel to provide quality care

Universal precautions

Working with Office Staff

Training personnel to provide quality care

Train all personnel who have contact with patients

Recognize inaccurate information regarding dangers
and problems associated with agonist therapy

1. Staff education and training should include all personnel who will have contact with patients (e.g., receptionists, nurses, billing staff).
2. There can be strong beliefs among staff about the use of medications for the treatment of opioid dependence. A discussion about such beliefs is warranted. It can be useful to talk about the use of nicotine products and bupropion (Zyban) for the treatment of smoking, and the use of medications for the treatment of alcoholism (e.g., naltrexone – ReVia). Point out that proper dosage levels of medications ensure that patients are obtaining full therapeutic benefits while not producing “highs” such as those obtained with illicit opioids (e.g., heroin).

Working with Office Staff

Staff education

Training personnel to provide quality care

Universal precautions

Working with Office Staff

Universal precautions

Staff should be trained and encouraged to use universal precautions with all patients

1. Finally, staff should be reminded to employ universal precautions – not just with patients being treated for opioid dependence, but all patients being seen in the office.

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1. Next, we'll review aspects of the first office visit made by the patient seeking treatment for opioid dependence.

Information for the Patient

Physician's name, address, phone number, office hours

Emergency contact information

Payment procedures

Copy of rules/expectations signed by patient

Information about buprenorphine (e.g., handout, brochure)

1. The patient should be given information such as the physician's name, address, phone number, office hours, emergency contact information, and payment procedures in writing.
2. Office hours and appointment times should be convenient – especially in the first days and weeks of treatment, when dose is being stabilized. Minimal waiting times and brief visits for dosing, might be planned.
3. If the patient lives in a rural area, or services are not available where the patient lives or works, then special accommodations for long travel distances might be made.

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1. Another topic that needs to be addressed with the patient at the first visit is the payment for services provided.
2. Notably, at this time (January, 2001) the cost for buprenorphine medication in the U.S. is not known.
3. The clinician should realistically establish how the patient will pay for treatment at the onset of treatment.
4. Decide upon a fixed fee per month versus individual billing of each service component (office visit, phone call, medication dispensed, urine test).
5. Do not assume that a patient who spends \$100 per day on heroin will be able to willing to spend \$25 per day on treatment.
6. Establish at the beginning of treatment what will happen if payment is delinquent.

Financial Issues

Financing of methadone treatment

Fees for office-based treatment

Ways patient may pay for treatment

1. In order to understand payment of services, it may be helpful to take a moment and consider how it may compare to financing of methadone treatment.

Financial Issues

Financing of methadone treatment

Paying for methadone treatment occurs through:

Out-of-pocket payments

Insurance reimbursement

Medicaid (in some states)

State treatment grants (in some states)

1. Payment for methadone treatment can occur through a variety of means. These mechanisms vary widely. Some programs will have several different reimbursement methods.

Financial Issues

Financing of methadone treatment

Fees for office-based treatment

Ways patient may pay for treatment

1. The physician will need to consider the fee for office-based treatment based in part on local costs.

Financial Issues

Fees for office-based treatment

Services that need to be considered when determining the fee for care include, among others:

- Routine office visits
- Record-keeping and billing
- Medications
- Counseling

1. Some of the services that may be provided to buprenorphine maintained patients are listed on this and the next slide.
2. The length of routine office visits may vary widely. The most stable patients may need brief visits (e.g., 15 minutes or less). Other patients may need more time, depending upon the status of their illicit opioid use, as well as other aspects of their lives.
3. If on-site treatment is to be provided (e.g., a weekly group run by a nurse, an office-based counselor), then the fee for such treatment services will need to be determined.

Financial Issues

Fees for office-based treatment (continued)

Services that need to be considered when determining the fee for care include, among others:

Urine testing

Physical examinations

Laboratory work

Financial Issues

Financing of methadone treatment

Fees for office-based treatment

Ways patient may pay for treatment

1. It is important for the office staff to determine how the patient plans to pay for treatment, and arrange to bill the patient directly or to bill a third party payer, or both.
2. The patient may have insurance that covers some but not all aspects of treatment (for example, an initial office visit with history and physical examination, regular office visits to monitor medications for chronic conditions, associated laboratory tests, etc., but not on-site substance abuse counseling).

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1. Finally, let's briefly discuss community relations as they relate to office management.

Community Relations

Discussing buprenorphine treatment with other local physicians

Talking to neighbors if necessary

Monitoring for loitering and instructing patients as needed

Cautioning staff about confidentiality when in the community

1. Treatment with buprenorphine in an office setting should be like treatment of other medical disorders. The decision to begin treating patients with depression or alcoholism would not typically involve a need to meet with others in the area to alert them of your plans. You may decide that there is no need to draw attention to your expansion of practice. However, you may choose to discuss your plan with others in order to avoid or ameliorate any negative response they may have. Experience with methadone maintenance treatment programs indicates that some people do not want a program that will bring opioid abusers to their neighborhood.
2. You may decide to discuss buprenorphine treatment with other local physicians (for example, if there are other doctors in your office building, or in nearby buildings).
3. You may choose to talk to neighbors. If so, explain that the number of patients you will be seeing will be small, and that they are patients who are stable.
4. Reinforce caution with staff that they should avoid any discussion about any patients in the community.

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- II. The initial visit
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Summary

The necessary resources should be in place before beginning office-based treatment with buprenorphine

It is vital to include all members of the office staff in the planning of, and training for treatment for opioid dependent patients with buprenorphine; periodic reviews with staff are useful, too

It is important to confirm how the patient will pay for treatment

Medical Record Keeping

Medical Record Keeping

Office-based Buprenorphine and Medical Record Keeping

The medical record is the ongoing narrative of a patient's healthcare and memorializes the past history for purposes of continuity of current and future treatment. Treatment for substance abuse is confidential. The medical record is a legal document which takes on different importance when a controlled substance – such as buprenorphine – is used in the treatment of substance abuse.

1. The medical record is a document that services both clinical and legal purposes.
2. The initial documentation in the record should include a complete history (discussed in more detail later in this talk), and results from the initial physical examination.

Office-based Buprenorphine and Medical Record Keeping

The purpose of this section is to review aspects of medical record keeping as they apply to treatment of patients with a substance abuse disorder. This is particularly important for office-based buprenorphine treatment, since there are specific legal aspects of record keeping and substance abuse treatment.

1. The medical record is a document that services both clinical and legal purposes.
2. The initial documentation in the record should include a complete history (discussed in more detail later in this talk), and results from the initial physical examination.

Outline for This Talk

- I. Overview to the medical record
- II. The history portion of the record
- III. Treatment plan
- IV. Documentation and buprenorphine
- V. Documentation scrutiny
- VI. Alteration of records
- VII. Storage of records
- VIII. Summary

1. This talk will review general aspects of medical record keeping, as well as specific issues associated with the treatment of opioid dependent patients (especially those treated with buprenorphine).

2. It is possible that regulations governing medical records may change – especially regulations pertaining to office-based buprenorphine treatment for opioid dependence. At present (January 2001), regulations exist that govern the storage and access of medical records for substance abuse treatment (e.g., who has access to the records, under what circumstances access to records is provided to others, where records are kept). These topics are covered in this talk, but it should be noted that such regulations may change. In addition, aspects of medical record keeping (e.g., what should be in the medical record, how corrections should be documented in the medical record) are included in this talk. These are features of good clinical practice and are not driven by regulations.

Outline for This Talk

- I. Overview to the medical record
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- VII. Storage of records
- VIII. Summary

1. We will begin with an overview to the components of the medical record.

[Reference:

Lopez, F. (ed) Confidentiality of Patient Records for Alcohol and Other Drug Treatment. Technical Assistance Publication #13, U.S. Department of Health and Human Services, Center for Substance Abuse Treatment, Rockville, Maryland, 1994.]

Overview to the Medical Record

The medical record should document

Initial diagnosis and treatment plan information

Complete history

Physical examination results

On-going history and physical examination

1. The medical record is a document that serves both clinical and legal purposes.
2. The initial documentation in the record should include a complete history (discussed in more detail later in this talk) and results from the initial physical examination.

Overview to the Medical Record

The medical record should document (continued)

Comparisons with initial presentation for progress or retrogress (with corresponding modifications, if needed, in the treatment plan)

Assessment of pharmacological efficacy

Lab tests and results

1. Other aspects that should be included in the medical record are shown on this slide.

Overview to the Medical Record

The medical record should document (continued)

Consults

Compliance with treatment plan

Urine and blood drug screening

Collection

Results

1. An assessment of the validity of urine specimen collection should be noted. This documentation should include:
 - a) Documentation of urine test
 - i) observance of specimen collection by a staff member
 - ii) immediate labeling of specimen with name or code number
 - iii) observance of temperature, specific gravity, pH, creatinine level, color and odor
 - b) Storage of specimen
 - i) length of time between specimen collection and performance of test
 - ii) refrigeration
 - iii) freezing
 - iv) split samples
 - v) isolation of refrigerator
 - vi) staff access to refrigerator
 - vii) sign-in/sign-out, date, time, initials
 - c) Laboratory
 - i) on premises or referral lab
 - ii) certification
 - d) Chain of custody/evidence
 - i) document above with initials or signatures of authorized personnel
 - ii) in cases of dispute, have two authorized staff members witness and sign-off

Overview to the Medical Record

The medical record should document (continued)

Medications prescribed

Inventory and dispensing of controlled substances

1. Finally, the medical record should include a listing of medications prescribed (including dates, strength, amounts, number of refills if possible).
2. If medication is being dispensed from the office, a record of this needs to be kept in the patient's record (in addition to a separate inventory record of medication kept in the office).

Outline for This Talk

- I. Overview to the medical record
- II. The history portion of the record**
- III. Treatment plan
- IV. Documentation and buprenorphine
- V. Documentation scrutiny
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1. Next, we'll review in more detail some of the particular elements of the history that should be included in the record of a patient being considered for office-based buprenorphine treatment.

History Portion of the Record

Much of what should be recorded by the admitting physician is normally gathered as a part of the initial interview with any new patient seen in the office setting

History Portion of the Record

Particular attention should be paid to documenting

Social supports and living arrangements

Employment status

Addiction and treatment history of patient and close family members

1. This is not meant to be an exhaustive list of all elements of the history, and much of this material is normally collected as a part of the routine history.
2. It is good to assess the social supports available to the patient – such as marital status, persons with whom the patient lives, and employment situation. It is also helpful to determine if these supports are available to actively aid in the patient's recovery.
3. Similarly, information about the patient's addiction and treatment history will help assess prognosis.
4. Abuse of drugs or alcohol by family members can also impact (and impede, if active) the patient's recovery.

History Portion of the Record

Particular attention should be paid to documenting
(continued)

Whether the patient has current medical or psychiatric conditions, and treatment status

How the patient intends to pay for treatment (especially if his or her insurance company is not to be billed)

1. Complicating medical or psychiatric conditions may make it more difficult to treat the patient in the office. It is important to document the assessment of whether these are acute or chronic, and to determine if the patient is in active treatment for them.
2. A frank discussion about paying for treatment needs to be held and documented in the chart at the first meeting.

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1. The treatment plan naturally grows out of the initial assessment of the patient.

Treatment Plan

The treatment plan part of the medical record should document:

Diagnoses and how determined

Treatment goals

Determination of medication to be used

How medication will be used

Psychosocial services needed/recommended

Signature of patient and provider

1. The treatment plan should include all of these elements. It should be reviewed with the patient, who should be included in the generation of the goals for treatment.
2. It is important to document a discussion with the patient about the use of medication (buprenorphine), how it is to be used (dosing, frequency), what can be expected from the medication, and what the medication won't accomplish (i.e., it is not a magic bullet).
3. The treatment plan should be reviewed with the patient, then signed and dated by the patient and the provider.

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1. There are some further points regarding medical record keeping that are particularly pertinent to use of buprenorphine.

Documentation and Buprenorphine

When planning to prescribe buprenorphine for opioid dependence treatment, it is important to document

Evidence showing patient is opioid dependent

Length and severity of patient's opioid dependence

Number, type, and intensity of previous treatments for opioid dependence

Any legal consequences to the patient because of opioid use

1. Don't forget that the record should indicate the reasoning used to derive a diagnosis of opioid dependence. This could include the frequency of opioid use, withdrawal when the person does not use, previous opioid withdrawal treatments (e.g., inpatient detoxifications), a DSM-IV diagnosis of opioid dependence, and legal involvement because of opioid use. Evidence from the physical examination may also support active opioid use (e.g., withdrawal in the office, needle marks).
2. It may be possible to begin persons on buprenorphine even if they are not dependent on opioids – for example, because they are at high risk for relapse to dependence. If such a situation occurs, it is extremely important to document the reasons for starting buprenorphine.

Documentation and Buprenorphine

Prior to starting the patient on buprenorphine, obtain and document the patient's consent

Document each of the elements of informed consent

Adequate information given

Patient competent to process information

Consent given freely and voluntarily

1. These elements of informed consent are not unique to treating a patient with buprenorphine.

Documentation and Buprenorphine

As a part of informed consent, document that you have

Notified the purpose of the treatment

Identified the agent to be used, what it does

Explained contraindications to use of the medication

Provided any special warnings, adverse reactions, side effects, drug interactions

1. The contraindications, side effects, drug interactions, and adverse reactions with buprenorphine are reviewed in other lectures.

Documentation and Buprenorphine

As a part of informed consent, document that you have
(continued)

Discussed dependence, withdrawal

Discussed alternative treatments

Determined who else can know about the treatment

1. Maintenance on buprenorphine does result in physical dependence, and discontinuation can result in a withdrawal syndrome (although buprenorphine's withdrawal syndrome is probably mild in intensity).
2. Alternatives to office-based buprenorphine treatment include clinic-based treatments with methadone or LAAM, as well as medically-supervised withdrawal and agonist-free treatment (that can include naltrexone).
3. Who else can know about the patient's treatment for opioid dependence? You should have the patient sign releases of information if he or she wants you to talk to others about the treatment. Be clear in the consent about what can and cannot be discussed.

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1. The medical record is valuable in the clinical management of the patient.
2. In addition, it serves an important function legally. The next several slides address various entities which have or can get access to the medical record. These are some of the legal aspects of documentation and records.

Documentation Scrutiny

Pertinent federal review groups and regulations

Pertinent state review groups and regulations

Insurance companies

1. The medical record may be reviewed by several different entities. Regulations regarding such reviews can exist for some governmental agencies (at the federal, state, and local levels).

Documentation Scrutiny

Federal review groups can include

Department of Health and Human Services (HHS):

Food and Drug Administration (FDA)

Substance Abuse and Mental Health Services
Administration (SAMHSA)

Department of Justice (DOJ):

Drug Enforcement Administration (DEA)

Federal Bureau of Investigation (FBI)

U.S. Attorney Offices

1. Federal groups that can review records include the FDA, SAMHSA (the Center for Substance Abuse Treatment – CSAT), DEA, FBI, and other offices.
2. The FDA and DEA can review records to ensure compliance with regulations.
3. The FBI can look at records as part of investigations of Medicaid or Medicare fraud, drug trafficking and other criminal acts.

Documentation Scrutiny

Pertinent federal regulations include

Confidentiality and disclosure of records

Storage and dispensing controlled substances in an office setting

Writing of prescriptions

1. There are a variety of regulations governing medical records, especially as they pertain to substance abuse treatment.
2. Patient confidentiality regulations have been reviewed in another section.
3. When writing prescriptions, remember to:
 - a) date and sign on the day issued
 - b) include the full name and address of the patient
 - c) include the full name, address, and DEA registration number of the prescriber
 - d) include the name of the medication, dosage form, strength, quantity prescribed, and directions for use
 - e) signature in ink, by the prescriber

Documentation Scrutiny

Pertinent federal review groups and regulations

Pertinent state review groups and regulations

Insurance companies

1. Besides federal review groups and regulations, there can also be state review groups and regulations.
2. For example, the criminal justice division of the state Office of the Attorney General may become involved for cases of Medicaid or Medicare fraud. State medical boards can become involved as well, if improper practice is alleged.

Documentation Scrutiny

Pertinent state regulations

Typically modeled on federal template

Can be more stringent than federal regulations

Subpoena may be required

1. State regulations vary from state to state and need to be known by the practitioner.
2. The agency or review group may be required to obtain a subpoena.

Documentation Scrutiny

Pertinent federal review groups and regulations

Pertinent state review groups and regulations

Insurance companies

1. Insurance companies may become involved in reviewing medical records.

Documentation Scrutiny

Insurance companies

May seek to review medical records to determine the medical necessity of treatment provided

1. These reviews may seek to determine if treatment was “medically necessary.”
2. The insurance company is required to have the patient’s consent for disclosure of treatment. If the disclosure to the insurance company includes information about substance abuse treatment, then the consent must contain the appropriate elements (as specified in the Code of Federal Regulation (42 CFR Part 2). A sample consent is included in the Appendix of this section.

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1. How to make changes in the medical record is probably a familiar topic, but it is important and worth briefly reviewing and emphasizing.

Alteration of Records

Records can be legitimately changed under certain conditions

Words crossed out (not erased)

Date and initials of writer entered at correction site

New or changed information inserted

Investigators and attorneys are trained to detect aberrations

1. Make sure that the medical record is neat and legible.
2. Never erase or white out anything written in the records.
3. Put a single line through an error, date and initial the area of change.

Alteration of Records

Absence of words or information is construed as never existing

Controlled substance records are more likely to be scrutinized due to addiction and diversion

1. If it isn't documented, then it hasn't happened. Document carefully what is being done.

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1. Lastly, we will briefly review the current regulations regarding storage of records.

Storage of Records

Must keep available for at least 2 years

Can be kept at a central location (but must notify DEA)

Must be kept in a locked, secure place when not in use

1. Currently, DEA regulations require maintenance of records for at least 2 years. State regulations or accrediting bodies may require longer periods.
2. Records do not need to be kept on site, but if they are moved off site then the DEA needs to be notified.

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Summary

Documentation and immaculate record keeping are extremely important – for the well being of both the patient and the physician.

The record is a legal document that may be reviewed by outside agencies.

Appendix to
Medical Record Keeping:

Sample Consent Form for
Release of Confidential Information

Sample Consent Form Release of Confidential Information

I, _____ (name of patient),

authorize _____

(name or general designation of program making disclosure)

to disclose to _____

(name or person or organization to which disclosure is made)

the following information:

Sample Consent Form Release of Confidential Information (continued)

The purpose of the disclosure authorized herein is to:

(purpose of disclosure, as specific as possible).

I understand that my records are protected under the Federal regulations governing Confidentiality of Alcohol and Drug Abuse Patient Records, 42 CFR Part 2, and cannot be disclosed without my written consent unless otherwise provided for in the regulations.

Sample Consent Form Release of Confidential Information (continued)

I also understand that I may revoke this consent at any time except to the extent that action has been taken in reliance on it, and that in any event this consent expires automatically as follows:

(specification of date, event, or condition upon which this consent expires)

Signature of patient: _____

Signature of parent, guardian or authorized representative when required: _____

Date: _____

Notice with Release of Information Consent

This notice accompanies a disclosure of information concerning a patient in alcohol/drug abuse treatment, made to you with the consent of such patient. This information has been disclosed to you from records protected by Federal confidentiality rules (42 CFR Part 2).

Notice with Release of Information Consent (continued)

The Federal rules prohibit you from making any further disclosure of this information unless further disclosure is expressly permitted by the written consent of the person to whom it pertains or as otherwise specified by 42 CFR Part 2. A general authorization for the release of medical or other information is NOT sufficient for this purpose. The Federal rules restrict any use of the information to criminally investigate or prosecute any alcohol or drug abuse patient.

Case Illustrations

Case Illustrations

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Cases #1 - #8 were prepared for the workshop given by the California Society of Addiction Medicine on October 6, 1999 as part of the conference: State of the Art 1999 – Evidence-based Addiction Medicine, at the Marina Beach Marriott Hotel in Marina del Rey, California.

CASE #1 – Lawyer, beginning to use daily

Mr. Smith is a forty-year-old male who comes to your office asking to be treated with buprenorphine. Mr. Smith is a criminal defense attorney in private practice, and he knows about buprenorphine because you are treating some of his clients. His goal is to use buprenorphine during the week and occasionally use heroin (by snorting) on the weekend. He has used heroin for the past 5 years.

For the past 6 months, he has used heroin primarily on the weekend, but he is concerned now because he has begun to use small amounts of heroin daily. If he doesn't use heroin, he gets loose stools, is irritable, and has difficulty getting and staying asleep. He has no desire to completely stop heroin use, but he doesn't want to use it during the week.

His passion is playing jazz and he has organized a band. He says that heroin use is common in the club where his band plays. All the members of the band use heroin and many of his friends who come to the club also snort or inject heroin. He rarely buys heroin, as his friends usually give it to him.

His only other drug use is marijuana and alcohol (3-6 drinks/night on the weekend), again primarily used on the weekend. He has never been arrested or had significant medical consequences from his heroin use. He is not married. He has a 14-year-old son who he has supported and sees often.

What is the diagnosis?

Is this patient a candidate for treatment with buprenorphine?

What are the treatment goals?

What is the initial treatment plan?

CASE #2 – 16-year-old younger brother

A 16-year-old begins occasional iv heroin use with his older brother. Everyone in his circle of friends uses heroin but no one uses it daily. In their circle, guys who get addicted are losers who can't handle their dope.

Occasional heroin use is not uncommon in their community and among his friends. The older brother injects the younger one.

One day, the older brother injects them both with the same amount of heroin, but the younger one lapses into coma. He is taken to an emergency room where he receives Narcan and is released. Both brothers are frightened by the experience and vow to stop using, which they do for six weeks.

When the older brother moves away, the younger brother is arrested making his first street buy and spends a week in the county jail. As soon as he gets out of jail, he uses heroin — which surprises him. While awaiting trial, his attorney advised him to seek drug abuse treatment and to “stay clean.” He comes to you asking for help.

What is the diagnosis?

Is this patient a candidate for treatment with buprenorphine?

What are the treatment goals?

What is the initial treatment plan?

CASE #3 – 37-year-old man wanting to withdraw from methadone

A 37-year-old man came to the clinic asking to be given buprenorphine to help him withdraw from methadone.

He had been in a methadone maintenance treatment program for the last 9 years. Before that, he had a 5-year history of heroin use; two years of which were iv use. During his first year of methadone maintenance, he had used heroin occasionally, but after that he had been abstinent from heroin use for 8 years.

He has been employed for the past 12 years in the same job. He is HIV negative. He has been in a stable relationship with a non-drug-using partner for the last 7 years. He wanted to discontinue methadone maintenance, and in preparation he had reduced his dose to 30 mg.

What is the diagnosis?

Is this patient a candidate for treatment with buprenorphine?

What are the treatment goals?

What is the initial treatment plan?

CASE #4 – 19-year-old university student

Part I

A 19-year-old female university student comes to you asking for treatment of her heroin use. She has been smoking heroin for the last 15 months, and smoking daily for the last 3 months. She is now using 1½ grams a day. Some of her friends are now switching to iv use because it takes less heroin to keep from getting sick. She says she does not want to do that but may be “forced” to because she cannot keep paying the “extra cost” of smoking. She has used all the money her parents gave her for school expenses to buy heroin, her credit cards are maxed out, and she has borrowed money from her friends. Until last semester, she had an overall B average, but this semester she is in academic difficulty. When she doesn’t use heroin, she has muscle aches, diarrhea, insomnia, and anxiety. She recognizes the symptoms as heroin withdrawal and was surprised because thought she could not develop dependence by smoking. She has no prior history of drug treatment.

What is the diagnosis?

Is this patient a candidate for treatment with buprenorphine?

What are the treatment goals?

What is the initial treatment plan?

Part II

The clinic physician gives her a prescription for 6 day supply of buprenorphine (4 mg/day), and she is told to participate in the clinic’s relapse prevention workshop six days a week and to schedule individual counseling at the clinic once a week.

She returns 3 days later having taken 8 mg/day for 3 days. She has not attended the relapse prevention workshop nor scheduled an individual counseling session. The counselor is not available to see her when she comes

What is the treatment plan at this point?

Part III

She returns the following day at a time when neither the group nor the counselor is available. She is told she has to attend the relapse prevention workshop in order to get medication. She does not return to the clinic for 4 weeks. When she does, she is smoking more heroin than before, but having no difficulty with finances because she has dropped out of school and is working as a stripper at a local “gentlemen’s club.”

What would you recommend at this point?

CASE #5 – 42-year-old taking Vicodin from his orthopod

A 42-year-old male is using about 20 Vicodin tablets/day, which he obtains from his orthopedist and his family practice physician. He attends AA meetings sporadically, but has an eastern religious orientation and doesn't like all the "God stuff." He has also attended SOS and rational recovery meetings, but they are too "intellectual." Whenever he drinks alcohol, he soon spins out of control, and he accepts that he is alcoholic. He believes that the pills have caused him no problems except for the hassle of conning doctors into prescribing as many as he wants. He has stopped using pills on two occasions. About 2 years ago, he tapered himself down to 5 Vicodin tablets/day. He felt awful and began drinking. A month later his wife was threatening to leave him unless he got treatment for his alcoholism. He was drinking daily and had to have a drink in the morning so he could shave without cutting himself.

He had an uneventful detoxification and entered an outpatient drug abuse treatment program. He stopped drinking, but unknown to the program, resumed his use of Vicodin. A year later he again stopped Vicodin use and resumed alcohol use, but he saw a psychiatrist who gave him some Vicodin so he wouldn't use alcohol. He successfully stopped use of alcohol.

Although he has shoulder and knee pain from a skiing injury, he is aware that he uses Vicodin as a "cocktail" when he gets home in the evening, and to deal with his kids after a stressful day at work. He also uses 4-6 Vicodin in the afternoon to allay fatigue and irritability. He says that no one, including his wife, knows of the extent of his Vicodin use; and even his wife, who knows immediately if he has used alcohol, cannot tell when he is using Vicodin. He says that his orthopedist has cut him off, and his family physician is getting "testy" about his requests for Vicodin. He has tried to order Vicodin and Codeine from off-shore pharmacies on the Internet, and has tried to purchase tablets on the street, although he has been successful at neither. He cannot imagine life without Vicodin or some opiate. He seeks treatment with you because he says that getting Vicodin from a psychiatrist, who will only prescribe it if he is in weekly psychotherapy, is way too expensive.

What is the diagnosis?

Is this patient a candidate for treatment with buprenorphine?

What are the treatment goals?

What is the initial treatment plan?

CASE #6 – Chronic back pain

Mr. Martin is a 52-year-old patient who has been using Duragesic 100 ug, Norco 10 tablets/day and Oxycontin 40 mg four times/day for the past year for treatment of chronic back pain. Mr. Martin has been taking medications as prescribed, except that he occasionally takes extra Norco during periods of extremely high pain. He also takes less when the pain is lower.

Mr. Martin has been in recovery from alcohol dependence for 20 years. He is well versed in AA, but doesn't attend meetings now because he has difficulty sitting for more than a few minutes. He has abused no other drugs.

Medical problems include obesity, hypertension, and depression. He is on medication for blood pressure and Wellbutrin SR, 300 mg/day. His symptoms are particularly severe in the morning and "getting started" takes him two to three hours. He usually takes his first round of pills immediately on awakening and three days a week (on days that he is changing the Duragesic patch) he spends an hour in the hot tub. His morning routine includes reading, stretching, and walking before he drives to his office. He seeks addiction medicine consultation because he is concerned that his narcotic use is getting too high and that he is now addicted to pain medications.

What is the diagnosis?

Is this patient a candidate for treatment with buprenorphine?

What are the treatment goals?

What is the initial treatment plan?

CASE #7 – Nurse who took Vicodin

Part I

Mrs. Jones is a 35-year-old nurse and mother of three small children (age 3, 5, and 6) who comes to your office in a very distressed state. She used intravenous heroin between ages 15 and 25. She has been in recovery for 10 years. While she was abstinent, she was periodically depressed and was treated with Prozac 20 mg/day, which improved her depression. She is employed by a HMO as a case manager in a drug abuse treatment program. Her husband, also in recovery from heroin and alcohol dependence, is currently in jail for non-drug abuse related assault. She stopped using heroin after she discovered that she was hepatitis C positive. During her recovery, she attended AA or NA frequently until her husband went to jail. Her mother, who is ill with cancer, lives with her. Four days before coming to your office, one of her patients had given her a prescription bottle containing about 100 Vicodin tablets. Mrs. Jones had taken all the Vicodin tablets. Earlier in the day, she had left work because she was having severe diarrhea. She said that she couldn't afford to be "junk sick" now because this afternoon she had to take care of her children and her mother.

What is the diagnosis?

Is this patient a candidate for treatment with buprenorphine?

What are the treatment goals?

What is the initial treatment plan?

Part II

Mrs. Jones was prescribed .1 mg of clonidine every 4 hours for three days, administered one mg of Klonopin, and told to take one tablet of Imodium following each loose stool. She took the following three days off work. Although the acute symptoms of diarrhea resolved over the next two days, she said she continued to feel anxious, inexplicably sad, and have difficulty sleeping. She craved opiates and constantly schemed of ways of getting them, including phoning in prescriptions for her. Three weeks later, the same patient gave Mrs. Jones another bottle of Vicodin. Mrs. Jones was clear that she cajoled her patient into "turning over" the Vicodin. Mrs. Jones said that she wanted the Vicodin so bad she could "taste it." She resolved to ration the Vicodin at 6/day, but once she started taking them, she used them all over 4 days and again presented in crisis. She said she couldn't miss work again and wanted buprenorphine detoxification.

What is the treatment plan now?

Part III

Her attending physician treated her with 1 mg buprenorphine four times/day for one week, then began to taper buprenorphine one tablet/week. When she dropped to 3 mg/day, she said that she felt extreme anxiety after 3-4 hours and increased her dose back to 4 mg/day. She said that when she was taking 1 mg four times/day she felt normal: "not high," or "loaded" like when she was on Vicodin, but alert and able to cope with her job and family responsibilities. She wants to continue on buprenorphine four times/day dosing for at least the next six months "while I get myself together." She was referred to a psychiatrist for evaluation. The psychiatrist diagnosed her as having an agitated depression and, in view of her previous response to Prozac, prescribed Prozac 20 mg/day.

What is the treatment plan now?

CASE #8 – 42-year-old man in a posh hotel

Day I

After a number of phone discussions with his attorney, you sit across from your prospective patient at a posh hotel in Beverly Hills.

“You come highly recommended,” he says. He stands up and walks to the window of his hotel room, keeping his back to you as he speaks. “For your discretion as well as your skills treating addiction. As you may have surmised from talking with my attorney, it is of the utmost importance that no one know that I am under your care.” He turns and intently watches your response.

“Who referred you?” you ask.

“Natasha, a woman you treated several years ago from my country. She sends her regards, by the way, and wanted me to let you know that she is still clean.”

“How long have you been addicted to heroin?”

“So you don’t know Natasha. OK, I like that. I have smoked heroin on and off for 10 years, but have stopped for months at a time when it was necessary to do so for business reasons. This is the first time that I’ve not been able to stop on my own. I’ve been smoking it every day for six months.”

“Do you use only by smoking?”

“Heroin, yes. I only smoke it. I got morphine from a doctor in London, but I was never addicted to it. In fact, I had to have him or his nurse shoot me up, I can’t stick myself with a needle.”

With additional questions you learn the following. He is 42-years-old and married. His wife and two daughters live in Moscow. His attorney, two bodyguards, and pilot occupy rooms adjoining his suite. He has no medical problems except for hepatitis C, that he says he got from a blood transfusion following a motorcycle accident in Morocco 10 years ago. He has had a course of interferon from a liver specialist in London, which made him quite ill and tired. He wants to be detoxified with buprenorphine and refuses to go to a hospital or to have any form of addiction treatment other than meeting with you daily in his room for “as long as you think necessary.”

You know that his name is Adrik, but he is vague about his work except that he is a “businessman.”

When he doesn’t smoke heroin for 12 hours, he becomes diaphoretic, has stomach cramps, can’t sleep, and says he feels like “I’m going to explode.” To stop these symptoms, he smokes heroin. He has tried to gradually cut back, but when he smokes, he always uses more than he intends and he realizes that “I can’t do it on my own.” He expects to stay in Los Angeles for about 10 days.

What is the diagnosis?

Is this patient a candidate for treatment with buprenorphine?

What are the treatment goals?

What is the initial treatment plan?

What questions does interaction between this patient and physician raise?

Day 2

You ask Mr. Adrik not to smoke any heroin the following morning so he will be in opiate withdrawal when you arrive at 10:00 AM. He does as you request. When you arrive, he is anxious and diaphoretic. You give him a 2 mg tablet of buprenorphine to hold under his tongue. After twenty minutes, he says “That’s pretty amazing stuff, I’m beginning to feel normal – not high, just normal.”

After he is feeling better, you examine him. His blood pressure is 140/90, pulse 98 and regular. You judge his pupils to be about the right size for the lighting conditions of the room. Neurological exam is normal. Lungs are clear and the liver is neither tender nor palpable.

He tells you that his pilot has reported a problem with the aircraft and that he will be staying in Los Angeles about 2 weeks while it is being repaired. He says he would like to continue to meet with you until he leaves.

Mr. Adrik gives you a bag containing some white power. “OK, doc, this is the last of my stash.”

You administer him another 2 mg buprenorphine tablet, and leave a 2 mg tablet for him to take at bedtime if he is experiencing withdrawal.

What questions are raised by this physician/patient interaction?

Day 3

“Rough night, doc. I took the tablet you left about 10:00 pm. Woke up in a cold sweat, sheets drenched at 4:00 this morning, so I smoked a joint to try and get back to sleep. Never did though. Not as bad as yesterday, but close.”

You administer two 2 mg tablets. As on the previous day, he reports feeling much better after about 20 minutes.

You ask him about the marijuana. He says he didn’t mention it to you because he doesn’t consider marijuana a real drug, like heroin or cocaine. “I just use it to sleep and sometimes for sex.” He denies having other drugs and makes no offer to give you his remaining marijuana. When asked for it, he says he wants to keep it “for emergencies.”

You ask him why he needs bodyguards. “Sometimes the competition gets a little rough, you never know. Besides, they do research. Nigel, who you met the other day in the hall, used to be an FBI spook. He checked you out before I came. He probably knows more about you than your mistress that lives in an apartment on Wilshire, or probably, for that matter, a lot more than your wife.”

Before you leave, you administer another 2 mg buprenorphine tablet and leave another 2 mg tablet to be taken at bedtime.

What questions are raised by this physician/patient interaction?

Day 4

Nigel stops you in the hall before you get to the room. “Glad you’re here, doc; we can’t wake him.”

He ushers you into the bedroom. Mr. Adrik is ashen color. Respirations are about 4 per minute and shallow. He does not respond to shaking. When you put pressure on his sternum, he pushes your hand away. His chest is clear. His pupils are small, but not pinned.

You administer .2 mg of nalmeferone by intravenous injection. Within seconds, Mr. Adrik sits up in bed. “Son of a bitch,” he says, “I was having a great dream and you woke me up.”

He acknowledges having smoked heroin after he awoke during the night in a cold sweat. He said the usual amount of heroin had little effect so he had to smoke a lot, but he was finally able to get back to sleep.

You talk with him for 20 minutes or so. He is irritable and curt, but his thought processing remains clear. You administer a 2 mg tablet of buprenorphine. About 20 minutes later, he begins shaking and soils himself in the bed.

Over the next hour, he continues to sweat profusely and complain of being in withdrawal. You give him an 8 mg tablet of buprenorphine. After an additional 20 minutes, his chills and sweating subside.

You ask him where he got the heroin. He says he found a small bag in a pocket of a suitcase. He gives you the remainder of it. “I’m sure that is the last of it.”

You leave an 8 mg tablet of buprenorphine to be taken at bedtime. When you call him mid afternoon, he reports feeling “pretty good.”

What questions are raised by this physician/patient interaction?

CASE #9 – Subpoena

As you sit down at your desk on the Monday morning after a weeklong vacation trip, you find your mail stack about as high as you expected. As you glance through the pieces, you find an unusual one: a subpoena for all the medical records for John Williamson, your patient of 5 years.

Three months ago, Mr. Williamson had told you of his weekend use of heroin, explaining that he had been smoking it with friends from work for several months. When he said that he had begun to smoke every other day and was experiencing sweats and shakiness by the evening of the days he does not smoke, you told him he should consider treatment for opioid withdrawal. He agreed and he completed treatment in 6 weeks with no complications. You have seen him once a week since his last dose of buprenorphine, and done two urine screens, which were free of opioids. He appears to be doing well. The last time you saw him he said he had lost his job, but was interviewing for another.

The subpoena is from a lawyer representing his former employer.

What is your first action in response to the subpoena?

CASE #10 – Office partners

Your preparations for accepting your first patients into your office practice for treatment of opioid dependence with buprenorphine have been underway for several weeks. As one of the last steps, you are holding a meeting with all of the office staff on a Wednesday afternoon to present them with the packet of information you prepared for them and a copy of the information you will give to patients.

You are expecting to begin accepting patients on the following Wednesday.

You have spoken with both your office partners several times about your plans. They have been generally supportive but noncommittal. They know that you work with methadone maintenance patients at the University Methadone Clinic, but they are not interested.

You have told them directly that they will have to cover the patients on buprenorphine just as they cover all your other patients and they did not object. You have told them you would give them the information they need, and they said, “Fine.”

They both come into the office during your staff meeting. You stop long enough to ask them to take a copy of the information materials, and you say that you have scheduled a 2-hour meeting with them for Friday to go over it.

One of them says nothing; the other says, “What do you mean, ‘go over it’? Why do I have to go over this? I don’t want to, and I don’t think I need to. All I’m going to be doing is covering them for one night a week and one week-end a month.”

How do you respond to your partner?

Do you call the referring colleague and tell her to find another place for her patient to go into office-based buprenorphine treatment, because you can’t accept him next Wednesday due to unforeseen circumstances?

Pre-Post Test Questions

Sample Pre-Post Test Questions

Basic and Applied Pharmacology

A. Buprenorphine's effects at the mu opioid receptor can be described as a:

1. full agonist
2. partial agonist
3. antagonist
4. partial antagonist

[correct answer: 2]

B. The following are typical signs and symptoms of spontaneous opioid withdrawal:

1. lacrimation, rhinorrhea, miosis
2. diarrhea, gooseflesh, seizures
3. yawning, mydriasis, sweating
4. constipation, dry mouth, rhinorrhea

[correct answer: 3]

C. Buprenorphine's affinity for the mu opioid receptor is:

1. higher than heroin's
2. the same as heroin's
3. lower than methadone's
4. the same as methadone's

[correct answer: 1]

D. Buprenorphine is metabolized by which cytochrome P450 enzyme system:

1. 2D6
2. 3A4
3. 1A2
4. 2C19

[correct answer: 2]

E. Naloxone has:

1. good oral bioavailability, but poor sublingual bioavailability
2. good sublingual bioavailability, but poor oral bioavailability
3. good parenteral bioavailability and good sublingual bioavailability
4. poor oral bioavailability and good parenteral bioavailability

[correct answer: 4]

F. The time course of spontaneous withdrawal heroin:

1. starts in the first 6 hours after last use, peaks in first 24 hours, and resolves in 3 days
2. starts 6-12 hours after last use, peaks 36-72 hours after last use, and resolves in 5 days
3. starts 12-24 hours after last use, peaks 48-96 hours after last use, and resolves in 7-10 days
4. starts 24-36 hours after last use, peaks 72-96 hours after last use, and resolves in 7-10 days

[correct answer: 2]

G. Caution should be used when prescribing which class of drugs with buprenorphine:

1. benzodiazepines
2. calcium channel blockers
3. ACE inhibitors
4. penicillins

[correct answer: 1]

H. Under which circumstances could an acute dose of buprenorphine precipitate withdrawal in an opioid dependent person:

1. low level of physical dependence
2. long time interval since last dose of mu agonist opioid
3. high initial dose of buprenorphine
4. maintenance on an opioid antagonist

[correct answer: 3]

Role of Non-Pharmacological Treatment

A. The American Society of Addiction Medicine Patient Placement Criteria, Second Edition (ASAM PPC-II) should be used to:

1. derive an initial substance abuse diagnosis for the patient
2. determine if the patient is suitable for buprenorphine maintenance
3. guide the appropriate level of service needed by the patient
4. determine the patient's medical stability

[correct answer: 3]

B. You have been seeing a patient weekly in your office, and treating him with buprenorphine maintenance for his opioid dependence. He continues to use illicit opioids, as evidenced by repeated opioid-positive urine samples. You have raised the dose of buprenorphine several times. The most appropriate next step in his treatment is:

1. discontinue office-based buprenorphine treatment by discharging since he has failed to respond to buprenorphine
2. discontinue office-based buprenorphine treatment by transfer to methadone treatment since he has failed to respond to buprenorphine
3. continue office-based buprenorphine treatment, counsel him to stop using illicit opioids, and accept his use of opioids has decreased
4. continue office-based buprenorphine treatment and refer to a partial hospitalization program since he has failed to respond to buprenorphine

[correct answer: 4]

Psychiatric Co-Morbidity

A. DSM-IV criteria for Major Depression include all of the following except:

1. delusional guilt
2. decreased concentration
3. anhedonia
4. change in sleep

[correct answer: 1]

B. You receive a call from the wife of a patient. He is a patient well known to you, who is chronically depressed. She reports that he had been talking of wanting to kill himself, and then locked himself in the bedroom and now won't respond to her knocks on the door. She can hear the television in the room, and she believes he is simply "acting up again," as he has a long history of threatening suicide but never acts upon these threats. You tell her:

1. to continue to knock on the door and get him to answer
2. ignore him and not reinforce his behavior by giving him attention
3. call the police for help
4. shut off the power and see if he comes out of the room once the television is off

[correct answer: 3]

Medical Co-Morbidity

A. The prevalence of HIV infection in injecting drug users is between:

1. 5-10%
2. 11-20%
3. 21-30%
4. 31-40%
5. 41-50%

[correct answer: 3]

B. A patient treated in your office is HIV positive. The patient admits to injecting opioids daily, and has been non-compliant with efforts to treat his HIV infection with medications. You should:

1. discuss with him a trial of buprenorphine for his opioid dependence
2. refer him to methadone treatment for daily supervision and treatment
3. admit him to the hospital for a supervised opioid detoxification
4. monitor his CD4 count and watch for AIDS defining illnesses

[correct answer: 1]

Special Treatment Populations

A. You have followed an opioid dependent woman who has done well maintained on daily buprenorphine/naloxone. She now presents you with a confirmed positive pregnancy test and reports she believes she is ten weeks pregnant. You should:

1. counsel her about teratogenic effects of buprenorphine and naloxone, and gently explore her feelings and thoughts about possible pregnancy termination
2. maintain her on buprenorphine/naloxone
3. switch her from buprenorphine/naloxone to buprenorphine
4. begin a buprenorphine/naloxone taper with the goal of being off buprenorphine/naloxone by the end of her first trimester

[correct answer: 3]

B. You have followed an opioid dependent man who has been maintained on buprenorphine/naloxone for over two years. He has done very well, with no illicit opioid use or other drug use. However, he has chronic low back pain. He has no evidence of pathology that can be corrected by surgery, and he has not responded to measures such as non-pharmacological treatments and non-steroidal anti-inflammatory drugs. To help manage this pain you should:

1. change his buprenorphine/naloxone from once daily to thrice daily dosing
2. increase his daily dose of buprenorphine/naloxone
3. continue buprenorphine/naloxone and start a low dose of a mu agonist opioid for acute pain control
4. switch him to methadone and start a low dose of a mu agonist opioid for acute pain control

[correct answer: 4]

Patient Assessment/Selection

A. DSM-IV criteria for substance dependence include all of the following except:

1. tolerance to the effects of the substance
2. a persistent desire to cut down or control use
3. continued use despite knowledge of having a physical problem that is likely to be caused or worsened by use
4. recurrent substance-related legal problems

[correct answer: 4]

B. Opioids that are abused include all of the following except:

1. heroin
2. methadone
3. nalmefene
4. hydromorphone
5. hydrocodone

[correct answer: 3]

Clinical Management

A. You have started a patient on daily buprenorphine for his dependence on heroin. During the first days of treatment a urine sample is collected and tests positive for opioids. You switch the patient to buprenorphine/naloxone, and increase the daily dose over the several days until the patient is maintained on 24/6 mg per day. Another urine sample tests positive for opioids on the tenth day of treatment.

1. The positive test indicates the patient is still using illicit opioids.
2. The positive test is due to carry-over from illicit opioid use that occurred before the start of buprenorphine/naloxone treatment
3. The positive test is due to the presence of buprenorphine in the urine
4. The positive test is due to the presence of naloxone in the urine

[correct answer: 1]

B. A patient calls your office and reports she has been robbed and that the thief took her prescription for a month's worth of buprenorphine/naloxone. She has been maintained on buprenorphine/naloxone for four months, and has had a previous episode when she lost a prescription. You have obtained several random urine samples from her, and all have tested negative for opioids. Her husband is actively using illicit opioids. You should:

1. require her to attend your office weekly for prescriptions
2. switch her to a Monday/Wednesday/Friday schedule of dosing, and require her to attend your office for each dose of buprenorphine/naloxone
3. give her another prescription and warn her that she risks termination from office-based treatment if she loses or is robbed of a prescription again
4. arrange for her transfer to a local methadone clinic

[correct answer: 1]

Patient Confidentiality

A. On a Friday you have a voice mail message asking you to contact the police, who report that there is a warrant out for the arrest of a man you recognize as one of your patients. He is accused of robbing a local bank. The patient has faithfully attended your office on the first Monday of each month for three years, and has been maintained on buprenorphine/naloxone. He is employed, and has reconciled with his wife and children after his years of drug use. You have collected random urine samples (usually about once every month), and all have been negative for all drugs of abuse. You expect him in the office the following Monday. You should:

1. Inform the police that he will be entering your building on Monday, and suggest they watch for him as he arrives
2. Inform the police that he has been highly stable in treatment, and that you do not believe they have the correct suspect
3. Refuse to acknowledge to the police that he is your patient, but tell them you will discuss the accusation with the person if he is your patient
4. Refuse to acknowledge to the police that he is your patient, but verify when asked that you see your opioid dependent patients on the first Monday of each month
5. Refuse to acknowledge to the police that he is your patient, and discuss the accusation with the patient when you see him on Monday

[correct answer: 5]

B. A patient can give consent for release of information about their substance abuse treatment. Which one of the following is an aspect of such consent?

1. The consent can be verbal or in writing
2. The consent is not needed for communicating with the patient's spouse
3. The consent must include the purpose of the release
4. The consent is required to transmit information to other components of the same treatment program

[correct answer: 3]

Office Management

A. A member of your staff reports that she was confronted in the parking lot of your office building by a patient recently started on buprenorphine/naloxone. She clearly saw the patient, as it was the middle of the day and he was within her arm's reach. The person attempted to take her purse, but she was able to pull it away as a car pulled into the lot and frightened the assailant away. Which of the following is correct?

1. You cannot contact the police unless the patient gives informed consent.
2. The staff member cannot contact the police and report the person by name, since she identifies the patient through his substance abuse treatment and thus she would be violating confidentiality
3. You can contact the police but not identify the patient by name
4. You can contact the police and identify the patient by name

[correct answer: 4]

B. Which of the following resources must be in place before starting office-based buprenorphine treatment?

1. Access to a methadone maintenance program
2. Access to a system for collecting valid urine samples
3. Access to a partial hospitalization program
4. A relationship with the local police

[correct answer: 2]

Medical Record Keeping

A. Medical records for treatment of a patient's substance abuse disorder can be reviewed by all of the following groups except:

1. the Food and Drug Administration (FDA)
2. the Drug Enforcement Agency (DEA)
3. the Federal Bureau of Investigation (FBI)
4. the local police

[correct answer: 4]

B. The Drug Enforcement Agency (DEA) requires medical records for treatment of a patient's substance abuse disorder must be kept for a minimum of

1. one year
2. two years
3. three years
4. four years
5. five years

[correct answer: 2]

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